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, 2023

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: 001-41747

Turnstone Biologics Corp.

(Exact name of Registrant as specified in its Charter)

Delaware	**83-2909368**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
9310 Athena Circle, Suite 300 La Jolla, California	**92037**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (347) 897-5988

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 ($0.001 par value)	TSBX	Nasdaq Global 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 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, 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 Exchange Act). YES ☐ NO ☒

The Registrant did not have an aggregate market value for the common equity held by non-affiliates of the Registrant on the last business day of its most recently completed second fiscal quarter because there was no public market for the Registrant's common equity as of such date.

The number of shares of Registrant's Common Stock outstanding as of March 5, 2024 was 23,099,335.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for the 2024 Annual Meeting of Stockholders, which will be filed with the Securities and Exchange Commission within 120 days after the registrant's fiscal year ended December 31, 2023, are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated.

Turnstone Biologics Corp.

FORM 10-K

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Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K and the information incorporated herein by reference contain forward-looking statements that involve a number of risks and uncertainties, many of which are beyond our control. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, these forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements as a result of various factors, including those set forth below under the caption "Risk Factors."

Forward-looking statements include, but are not limited to, statements regarding:

- our plans to research, develop and commercialize any product candidates;
- our ability to obtain and maintain regulatory approval of product candidates arising from our proprietary Tumor-Reactive T Cell therapies;
- our ability to obtain funding for our operations, including funding necessary to commence and complete the clinical trials, conduct additional manufacturing and conduct preclinical studies of any of our product candidates;
- the success, cost and timing of our research and development activities, including our ongoing and planned preclinical studies and clinical trials;
- the size of the markets for our product candidates, and our ability to serve those markets;
- our ability to successfully commercialize our product candidates;
- the rate and degree of market acceptance of our product candidates;
- our ability to develop and maintain sales and marketing capabilities, whether alone or with potential future collaborators;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party service providers, including our contract research organizations, or CROs, suppliers and manufacturers;
- the safety, efficacy and market success of competing therapies that are or become available;
- our ability to attract and retain key scientific and management personnel;
- our ability to attract and retain collaborators with development, regulatory and commercialization expertise;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act;
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates and our ability to operate our business without infringing on the intellectual property rights of others; and
- the impact of macroeconomic developments, including the ongoing conflict between Ukraine and Russia, the state of war between Israel and Hamas and the risk of a larger regional conflict, on our business and operations as well as the business or operations of our customers, manufacturers, research partners, and other third parties with whom we conduct business.

In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "positioned," "potential," "predict," "seek," "should," "target," "will," "would" and

other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions described in the sections of this Annual Report on Form 10-K titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this report. We discuss many of the risks associated with the forward-looking statements in this Annual Report on Form 10-K in greater detail under the heading "Risk Factors."

Risk Factors Summary

Below is a summary of the material factors that make an investment in our securities speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this Risk Factor Summary, and other risks that we face, can be found below under the heading "Risk Factors" under Part I, Item 1A of this Annual Report and should be carefully considered, together with other information in this Annual Report before making investment decisions regarding our securities.

- We have limited operating history, have incurred substantial net losses and anticipate that we will continue to incur net losses for the foreseeable future. We have no products approved for commercial sale, have never generated any revenue from product sales and may never be profitable.
- We will require additional capital in addition to the proceeds from our initial public offering, or IPO to fund our operations, and if we fail to obtain necessary capital on acceptable terms, or at all, we will not be able to complete the development and future commercialization of our current and any future product candidates.
- Our business is highly dependent on the success of our lead Selected TIL product candidate TIDAL-01, as well as our other current and any future product candidates. All of our product candidates will require significant additional preclinical or clinical development before we are able to seek regulatory approval for and launch a product commercially.
- If we fail to develop and receive approval for our existing or any additional future product candidates, our commercial opportunity could be limited which could adversely affect our business, results of operations and financial condition.
- Unfavorable global economic conditions, including any adverse macroeconomic conditions or geopolitical events, including the conflict between Ukraine and Russia, conflict in the Middle East, and recent bank failures affecting the financial services industry, could adversely affect our business, financial condition, results of operations or liquidity, either directly or through adverse impacts on certain of the third parties on which we rely to conduct certain aspects of our preclinical studies or clinical trials.
- Clinical development involves a lengthy and expensive process, with uncertain outcomes. We may incur significant costs and/or experience delays in completing, or ultimately be unable to complete, the development of our current and future product candidates, including our lead product candidates.
- Preclinical development is uncertain. Our preclinical programs may experience delays or generate unfavorable data, and may never advance to clinical trials, which would adversely affect our ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all, and any of these events would adversely affect our business, results of operations and financial condition.
- Our product candidates are based on a novel approach to the treatment of cancer, which makes it difficult to predict the time and cost of product candidate development.
- The manufacture of our product candidates is complex, and we may encounter difficulties in production, particularly with respect to process development, quality control, or scaling-up of any future manufacturing capabilities. If we, or any of our third-party manufacturers encounter such difficulties, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

- We face significant competition and if we fail to compete effectively, our business, results of operations and financial condition could be adversely affected.
- Negative developments in the fields of immuno-oncology and TIL-based immunotherapy could damage public perception of our product candidates and adversely affect our business, results of operations and financial condition.
- We have relied and expect to continue to rely on third parties to conduct certain aspects of our preclinical studies, to conduct our clinical trials and to conduct investigator sponsored clinical trials of our product candidates. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, comply with regulatory requirements or terminate the relationship, we may not be able to obtain regulatory approval of or commercialize any potential product candidates.
- The regulatory approval process for our product candidates in the United States, and other jurisdictions is currently uncertain and will be lengthy, time-consuming and inherently unpredictable, and we may experience significant delays in the clinical development and regulatory approval, if any, of our product candidates.
- Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.
- Intellectual property rights do not necessarily address all potential threats to our business.
- Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

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PART I

Item 1. Business.

We are a clinical stage biotechnology company focused on developing new medicines to treat and cure patients with solid tumors. Approved immunotherapies represent a significant advancement in the treatment of solid tumors, but many patients either do not respond or experience relapsed disease following an initial response. We believe the most significant challenge to creating curative immunotherapies in these patients is the low numbers of T cells that can recognize and attack the tumor, which we refer to as tumor-reactive T cells. To address this problem, we are pioneering a differentiated approach to tumor infiltrating lymphocytes, or TILs. We are developing next generation TIL therapies by selecting the most potent (meaning able to mediate an anti-tumor response) and tumor-reactive T cells, which we refer to as Selected TILs. Unlike other approaches that rely on standard "bulk TILs" that have demonstrated objective responses in clinical trials only in limited tumor types, we are developing our Selected TILs for potential treatment across the majority of solid tumors. We have three ongoing Phase 1 clinical trials for TIDAL-01, including a multi-site trial for the treatment of breast cancer, colorectal cancer, head and neck cancer and uveal melanoma, and two investigator sponsored trials with H. Lee Moffitt Cancer Center and Research Institute, Inc., or Moffitt, across colorectal cancer, head and neck cancer and both cutaneous and non-cutaneous melanomas. We discuss the nature of these investigator-sponsored trials, including how these trials differ from a clinical trial sponsored by our company, as well as our roles and responsibilities in these trials, in more detail below. We intend to provide an initial clinical update across these three trials in mid-2024. We are also actively advancing our preclinical pipeline programs including TIDAL-02, our next Selected TIL program, and our TIDAL-01 and viral immunotherapy combination program. We define objective response as a patient experiencing a partial response or complete response to any given therapy.

Solid tumors present a major burden to society, with high mortality and poor outcomes associated with more advanced disease. Several key factors, such as tumor heterogeneity (meaning differences in the characteristics, including variable tumor antigen expression, between cancer cells within a patient's tumor, between tumors within the same patient and/or between different patients' tumor(s)) and challenging tumor microenvironments, have made treatment of solid tumors more difficult than treatment of hematologic cancers. Immunotherapies that activate the immune system to enhance and/or create anti-tumor immune responses, such as immune checkpoint inhibitors, or ICIs, have improved outcomes for some patients. However, more than 85% of cancer patients fail to respond to ICI therapy. The effectiveness of ICIs is heavily dependent on the presence of tumor-reactive T cells that ICIs can reinvigorate, and many patients lack a sufficient number of T cells that recognize the target tumor. Therefore, we believe new treatments that can expand and enhance the patient's tumor-reactive T cells are needed.

TILs are a type of cell therapy that harness the patient's own immune cells to target their own tumors. TIL therapy involves the isolation of lymphocytes from the patient's tumor, expansion of the isolated cells outside the body, and then infusion of the cells back into the patient. TILs have the ability to penetrate, recognize, and kill cancer cells and offer potential to treat or cure solid tumors. Because TILs include an expansive breadth of lymphocytes that are specific to the patient's tumor antigens, we believe they have the potential to overcome tumor heterogeneity which often presents a significant challenge for other therapies. Clinical trials with standard "bulk TILs," the first generation of TIL therapy that involves isolation and expansion of all of the TILs in the tumor sample, have shown objective responses in clinical trials in limited solid tumor types.

To date, several hundred patients in the United States have received bulk TIL therapies, with the greatest success observed in metastatic melanoma. In metastatic melanoma patients refractory to ICI therapy, specifically, PD-(L)1 treatments (meaning monoclonal antibodies targeting the immune checkpoint PD-1), bulk TIL monotherapy has yielded objective response rates (meaning the percentage of patients experiencing a partial response or complete response in any given study) of approximately 30% to 50%, with complete response rates (percentage of patients with complete eradication of measurable disease in the patient and no new lesions) ranging from approximately 5% up to 20%. If a complete response lasts the lifespan of a patient, it would be considered as a cure – in general clinical practice patients are referred to as "cured" if they remain in complete response for greater than five years as the probability of their disease recurrence is low. Beyond metastatic melanoma, bulk TIL therapy has demonstrated therapeutic potential in a limited number of solid tumors, including squamous cell carcinoma of the head and neck, cervical cancer, and non-small cell lung cancer. We believe that the activity of TILs is driven by the subset of tumor-reactive T cells, and that the key limitation for bulk TILs is the small number and proportion of

tumor-reactive T cells that make up the bulk TIL product (reported median less than 3%, *Lowery et al., 2022*). We believe increasing the proportion and diversity of tumor-reactive T cells in a TIL product can expand the potential utility of TILs, if approved, to a greater breadth of tumor types, where bulk TILs have shown limited to no objective responses in clinical trials to date.

Our Solution: Selected TILs

We are developing next generation TIL therapies for the potential treatment of multiple solid tumors. To our knowledge, at present there are no therapies in clinical development that provide curative outcomes for the majority of patients in our chosen solid tumor indications. Our innovative Selected TIL approach focuses on selecting and expanding the most potent tumor-reactive T cells to overcome the limitations of bulk TILs. This approach expands upon work conducted in academia that demonstrated improved clinical responses for certain selected TILs in solid-tumor types where bulk TILs have shown limited to no objective responses in clinical trials to date. We are leveraging this work to establish a standardized manufacturing process for large scale production of our Selected TILs.

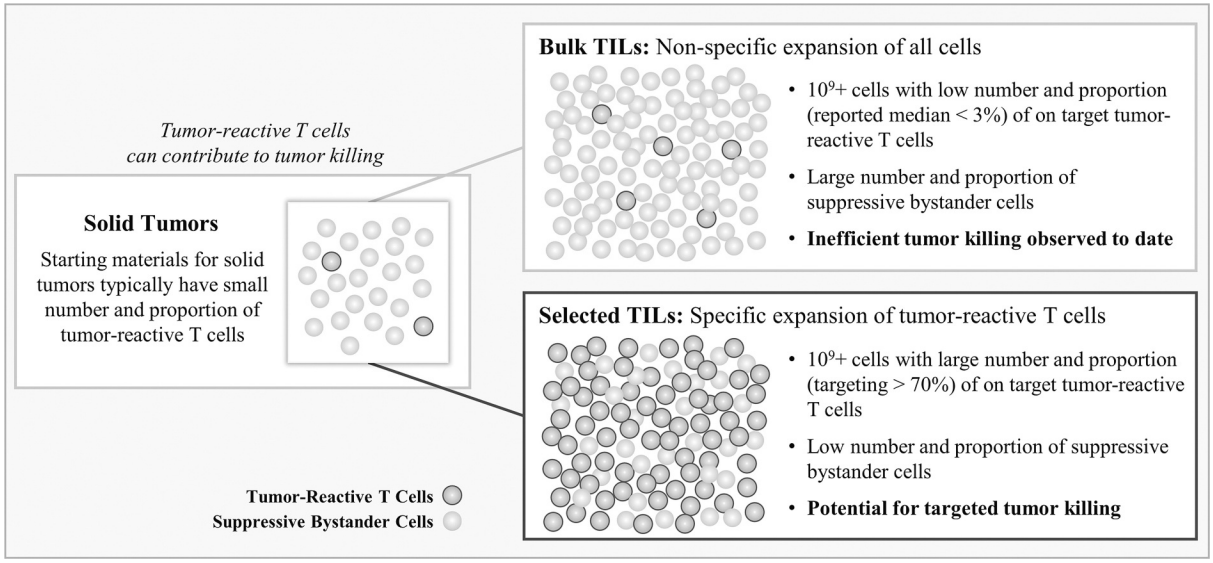
Our Selected TIL approach employs the following foundational principles with the goal of yielding the greatest number and proportion of tumor-reactive T cells in our TIL product candidates:

(1) *Unbiased identification of patient-specific tumor antigens:* We seek to identify the most comprehensive set of patient-specific tumor antigens. We use an unbiased identification process that aims to find and capture the greatest diversity of antigens with the potential to drive the most robust T cell response. Our proprietary approach is unlike other TIL products that are biased toward a specific subset or class of antigen(s), which may miss relevant tumor antigens or focus on the wrong targets.

(2) *Selection of greatest breadth of tumor-reactive T cells from patient extracted TILs:* Our goal is to capture and isolate the greatest number and proportion of a patient's tumor-reactive T cells that have the potential to attack and destroy heterogeneous solid tumors. We aim to select the greatest diversity of T cells by using a function-based screening process that confirms reactivity to the identified patient-specific tumor antigens rather than relying on a bioinformatics-based prediction algorithm that may not be truly predictive.

(3) *Expansion of tumor-reactive T cells and removal of non-tumor-reactive bystander cells:* We expand our selected tumor-reactive TIL population to magnitudes consistent with bulk TIL products and actively remove unnecessary bystander cells. This selective expansion resulted in a substantially higher proportion of tumor-reactive T cells in the final product in comparison to the relatively infrequent tumor-reactive T cells that are routinely found in bulk TIL. Based on our non-clinical studies across multiple tumor samples to date, we have been able to achieve tumor-reactive T cell frequencies in our Selected TIL drug product of up to 62%, with a median frequency of 23%. With ongoing continuous process improvements as part of our manufacturing strategy we are targeting >70% tumor-reactive T cells in our drug product as we advance clinical development.

The potential advantages of Selected TILs over bulk TILs are depicted in the figure below.



The Selected TILs approach described above is inherently designed to select for and characterize the active TIL product—the tumor-reactive T cells. Bulk TIL approaches do not select for the active TIL product and have consequently faced challenges in product characterization and potency assay development. We define potency as the specific ability or capacity of the product, as indicated by appropriate laboratory tests or by adequately controlled clinical data obtained through the administration of the product in the manner intended, to effect a given result. We believe that our Selected TIL approach has the potential to facilitate the development of potency release assays to support regulatory requirements and avoid the characterization challenges of bulk TILs.

Supporting Clinical Evidence

We believe the growing body of prospective and translational clinical data in the TIL field supports the potential of our Selected TIL approach. Third party studies have demonstrated that the anti-tumor activity of bulk TILs is driven by a small subset of tumor-reactive T cells in the bulk TIL product. Furthermore, clinical studies in academic centers utilizing rudimentary selection strategies for tumor-reactive T cells have reported responses including tumor regressions in a single patient bile duct study (*Tran et. al., 2014*) and a single patient colorectal cancer study (*Tran et. al., 2016*), one complete response and two partial responses out of six patients in a breast cancer study (*Zacharachis, et.al 2022*), and two complete responses and one partial response out of seven patients who received a TIL product with confirmed tumor reactivity, in a non-small cell lung cancer study (*Creelan et. al., 2021*). We define partial response as a patient experiencing a reduction in tumor size or volume as defined by the applicable standard, e.g. response evaluation criteria in solid tumors or RECIST, and no new lesions. A partial response does not indicate that a patient is cured of their disease.

Building a Product Pipeline to Further Enhance the Quality and Function of Selected TILs

Our Selected TIL approach sets us apart from others in the industry that are utilizing bulk TILs, including newer bulk TIL approaches that introduce genetic modifications and culture media additives to enhance TIL quality and function. We believe that without the optimal starting population of tumor-reactive T cells, further enhancements or modifications to bulk TILs are unlikely to succeed in extending their potential utility beyond the limited tumor types where bulk TILs have already shown objective responses in clinical trials. We are also expanding our product pipeline by making additional modifications to our proprietary Selected TILs and deploying them in differentiated combination strategies to further enhance TIL quality and function.

Modifications to Enhance TIL Quality

We are developing pipeline programs where we are evaluating enhanced culture conditions during the TIL production process to maintain and further improve TIL quality *ex vivo*. These enhanced culture conditions are designed to incorporate a mix of cytokines with the potential to rejuvenate dysfunctional and/or exhausted T cells.

Additionally, we plan to introduce functional genetic modifications into our pipeline programs that may drive potential for more sustained TIL quality and persistence, or ability of the TILs to survive and proliferate, *in vivo*. These gene edits will be designed to modify the tumor-reactive T cells to proliferate while resisting exhaustion post infusion, minimize their dependence on exogenous IL-2 for *in vivo* proliferation, and maintain their potential to kill tumors in suppressive tumor microenvironments. We are currently evaluating and prioritizing clinically informed targets for these genetic modifications.

Virus Combinations

Viral immunotherapy is a therapeutic modality with widespread potential to drive and modulate immune responses to solid tumors. Many viruses have inherent oncolytic activity that can be modulated through genetic engineering. These viruses preferentially infect, replicate within, and kill malignant tumor cells, and can induce broad immune responses. Viral immunotherapies are designed to convert immunologically unresponsive "cold" tumor microenvironments to more reactive "hot" tumor microenvironments and thereby enhance the activity of other immunotherapies.

We are strongly positioned to combine our Selected TIL products with our proprietary viral immunotherapies utilizing two distinct approaches:

- viral immunotherapy pre-treatment (prior to TIL extraction): optimize TIL harvest and broaden access to indications that are currently less amenable to generating effective TIL products; and
- viral immunotherapy post-treatment (following delivery of the TIL product): optimize TIL trafficking and function and further increase the activity of our TIL therapies, if approved.

Our Pipeline

We are applying our Selected TIL approach for the potential treatment of a wide range of solid tumors. We are developing a broad pipeline aimed at improving outcomes for patients, as illustrated in the chart below.

Programs		Product Overview	Key Indications	Preclinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestone
Selected TILs	TIDAL-01	Tumor-reactive Selected TILs	Breast cancer; CRC; HNSCC; Uveal melanoma					Initial clinical data in mid-2024
			CRC; Cutaneous and non-cutaneous melanomas; HNSCC	Moffitt Collaboration*				
		Combination with viral immunotherapy	Solid tumors					IND submission
	TIDAL-02	Selected TILs with next-gen manufacturing and TIL quality enhancements	Solid tumors					IND submission

* Two concurrent investigator sponsored trials at Moffitt Cancer Center

CRC - Colorectal cancer; HNSCC - Head and neck squamous cell carcinoma

We are advancing TIDAL-01, our lead Selected TIL product candidate, for the treatment of multiple solid tumor indications. TIDAL-01 utilizes an unbiased identification and functional screening process to isolate and selectively expand the greatest breadth of tumor-reactive TILs from the patient's tumor. Our TIDAL-01 production process is designed to deliver at least 10^9 cells and targets greater than 70% functional and potent tumor-reactive T cells. We have three ongoing Phase 1 clinical trials for TIDAL-01, including a multi-site trial for the treatment of breast cancer, colorectal cancer, head and neck cancer, and uveal melanoma, and two investigator sponsored trials with Moffitt across colorectal cancer, head and neck cancer and both cutaneous and non-cutaneous melanomas. Under our multi-site trial, we control all aspects of our trial including, but not limited to, study protocol development, patient selection and enrollment, regulatory interactions, data release, and manufacturing through our CDMO. Under the investigator sponsored trials, which are fully funded by us, Moffitt is solely responsible for regulatory interactions, trial conduct and manufacture of TIDAL-01 at the Moffitt Cancer Cell Therapy Facility, with input and support from us at Moffitt's discretion. Investigators at Moffitt are also solely responsible for the design of the trials and patient selection and enrollment, where we remain in close contact with the investigators to provide our input if appropriate. Any data disclosures will be made in collaboration with us and any improvements to the TIDAL-01 manufacturing process are solely at our discretion. We intend to provide an initial clinical update across these three trials in mid-2024.

Our next Selected TIL program, TIDAL-02, is being designed to encompass a next generation streamlined manufacturing process for tumor-reactive T cells and additional modifications to enhance TIL quality and function. We believe that TIDAL-02 has the potential to address the medical need in solid tumor indications that are distinct from and complementary to TIDAL-01. TIDAL-02 is currently in preclinical development.

We intend to evaluate the combination of TIDAL-01 with viral immunotherapy through two approaches: (1) treatment of the patient with viral immunotherapy prior to TIL extraction to optimize TIL harvest and broaden applicability to additional tumor types with low immune cell infiltration and (2) treatment of the patient with viral immunotherapy following treatment with TIDAL-01 to optimize TIL trafficking and infiltration into solid tumors and to support the anti-tumor functions of infiltrating immune cells. We are currently evaluating the optimal viral immunotherapy for combination with TIDAL-01 to advance into clinical development.

Our History and Team

We were founded in 2015 with the goal of developing medicines to treat and cure patients with solid tumors. Our initial scientific and technological focus was built around developing novel oncolytic viral immunotherapies. In late 2020, we acquired an innovative TIL platform and capabilities to expand our portfolio of cancer immunotherapies. Our TIL-based technology now represents the foundational therapeutic modality driving our current pipeline, though we continue to explore the synergistic potential of combining these two technologies in the pursuit of our mission.

We have assembled a team with extensive experience in complex biologics, drug discovery and development, manufacturing, and business and commercial product development.

We are led by our Chief Executive Officer, Sammy Farah, M.B.A, Ph.D., who has 20 years of scientific, business, and executive management experience in the biotechnology industry at Synthetic Genomics, Immune Design, Versant Ventures, and Merck.

Our experienced research and clinical development team brings a strong track record of advancing assets through clinical development and delivering products to the market. Our research organization is led by our Chief Scientific Officer, Stewart Abbot, Ph.D., who brings over 20 years of research and development experience in cell-based and immune-oncology products from Adicet, Fate, Celgene and GE Healthcare. Our clinical development and regulatory organization is led by our interim Chief Medical Officer, Michael Burgess, MBChB, Ph.D., who has more than 20 years of experience building research and development teams and leading strategy and execution of clinical development at SpringWorks Therapeutics, Bristol-Myers Squibb, Roche, and Eli Lilly.

Our chemistry, manufacturing, and control, or CMC, expertise and strategy is anchored in our in-house technical operations team with deep experience across bioprocess, analytical, and formulation development for complex biologics, with a proven track-record of enabling scalable, robust, and industrialized clinical and

commercial manufacturing processes and supply chains. Vijay Chiruvolu, Ph.D., our interim Chief Technology Officer who leads our technical operations organization, holds over 27 years of relevant industry experience in process development, manufacturing, supply chain, and quality at Instil Bio, Kite Pharma/Gilead Sciences, Scios, Avigen, Hoffmann-La Roche, Johnson & Johnson, and Amgen, and was responsible for the manufacturing and process teams that worked towards regulatory approval of two cell therapy products, Yescarta and Tecartus.

We believe that actively exploring and forming the right partnerships to drive innovation and enhance our pipeline is core to our strategy and growth. We have assembled a team with sophisticated business development expertise and capital formation experience to drive deal making and transactional activities. Our Chief Business Officer, Saryah Azmat, brings over 10 years of experience in biopharmaceutical business development, corporate strategy and capital formation at Bristol Myers Squibb and Putnam Associates. Venkat Ramanan, Ph.D., our Chief Financial Officer, holds over 20 years of experience in biopharmaceutical finance and operations at Seagen, Gilead, and Amgen.

Since our inception, we have raised $449.8 million in capital, including approximately $172.0 million from preferred stock financings and $190.0 million in non-dilutive payments from strategic partnerships and most recently, raised $80.0 million with gross proceeds from the IPO completed on July 25, 2023 and $7.8 million from the exercise of the underwriters option to purchase additional shares in the IPO.

Our Strategy

Our mission is to develop new medicines to treat and cure patients with solid tumors using our next generation TIL therapy approach. We intend to achieve our mission by implementing the following strategies.

- ***Advance our lead Selected TIL product candidate, TIDAL-01, for the treatment of solid tumors***. We are developing TIDAL-01 for the potential treatment of a broad range of solid tumor types and we are pursuing a clinical development strategy designed to demonstrate benefit in multiple indications. We have an ongoing Phase 1b clinical trial that will evaluate TIDAL-01 in solid tumors where the benefit of bulk TILs has not been established, including breast cancer, colorectal cancer, head and neck cancer, and uveal melanoma. Additionally, our two investigator sponsored Phase 1 clinical trials in collaboration with Moffitt that will evaluate TIDAL-01in colorectal cancer, head and neck cancer and multiple types of melanoma including cutaneous melanomas, an indication where bulk TILs have shown objective responses in clinical trials. We are very early in our development efforts, and as we make progress, if we obtain positive results of sufficient magnitude from one or more trial(s), we intend to discuss, receive guidance and the appropriate acceptance from the relevant regulatory agency(ies) to determine if we will be advancing TIDAL-01 into pivotal trials, which are trials that are intended to secure regulatory approval for a product candidate.
- ***Develop TIDAL-02 and continue to build our pipeline of additional Selected TIL programs.*** We are expanding our portfolio by making modifications to our Selected TILs to streamline manufacturing and further enhance the quality and function of Selected TILs. This strategy is exemplified by our second Selected TIL program, TIDAL-02. This program is intended to employ a next generation rapid selection process, culture enhancements to improve and maintain TIL quality *ex vivo*, and/or functional gene edits to ensure durable enhancements to TIL quality and persistence *in vivo*, while minimizing dependance on exogenous IL-2 for *in vivo* proliferation. We intend to advance TIDAL-02 towards the clinic for the treatment of solid tumor indications that are distinct from and complementary to TIDAL-01, with the goal of moving into earlier lines of therapy. In addition to TIDAL-02, we have ongoing research efforts to further expand our pipeline of Selected TIL programs.
- ***Leverage viral immunotherapies to further increase the activity of Selected TILs, if approved, across multiple solid tumors.*** Given our oncolytic virus expertise and our proprietary viral immunotherapies, we believe we are strongly positioned to be a leading company in using viral immunotherapy to further increase the activity of our TIL therapies, if approved. We plan to advance our TIDAL-01 and viral immunotherapy combination strategy to further expand the breadth and depth of response of our Selected TILs across multiple solid tumors. We also plan to explore additional Selected TIL and viral immunotherapy combinations.

- ***Commercialize and improve patient access to Selected TIL therapy through our CMC development expertise and manufacturing capabilities.*** We are expanding our in-house cell therapy process and analytical development capacity and capability, and in parallel assembling a network of external manufacturing and supply chain partners. We have designed a robust analytical characterization program to complement clinical development, support regulatory requirements and enable access to our Selected TILs for a broad range of patients with solid tumors. Our intent is that all early-clinical stage Selected TIL product candidates are built upon a CMC foundation with clear line-of-sight to commercial viability, sequenced and staged appropriately with clinical progress.
- ***Support existing and opportunistically explore future strategic partnerships and collaborations to maximize the potential of our programs.*** We are leveraging relationships with three academic collaborators, including a strategic partnership with Moffitt, and collaborations with the National Cancer Institute, or NCI, and Centre hospitalier de l'Université de Montreal, or CHUM, to help support development of our Selected TIL approach and pipeline. Our academic relationships are designed to enable us to tap into the deep expertise within these leading institutes that have decades of research and clinical experience in developing TIL therapies. We plan to continue to explore opportunistic collaborations with both academic and industry partners to extend our reach and maximize the potential of our programs.

Background on Solid Tumors and TILs

Solid Tumors: A Medical Need in Cancer

Solid tumors contribute a massive burden to society, with high mortality and poor outcomes associated with more advanced disease. In the United States, there are over 1.6 million new solid tumor cases per year, representing approximately 90% of all cancers. Furthermore, solid tumors result in over 500,000 U.S. deaths per year. Several key factors such as tumor heterogeneity, as well as challenging tumor microenvironments, have made solid tumors very difficult to treat. Despite advances in the oncology treatment landscape, solid tumors continue to result in low rates of long-term survival in the United States. When tumors become refractory to early lines of treatment, options for further therapy are currently limited to alternate forms of chemotherapy, clinical trials of agents in development or palliative care. Each of these alternatives presents a low likelihood of cure, while generally exposing patients to safety and tolerability concerns. Once the cancer metastasizes, mortality exceeds 90%.

Overview of Current Cancer Immunotherapies and Limitations

Immuno-oncology is an evolving field of cancer therapy that is designed to harness the power of the body's own immune system to prevent, control, and eliminate cancer. Immuno-oncology therapies activate the immune system to enhance and/or create anti-cancer immune responses, as well as to overcome immunosuppressive mechanisms that cancer cells have developed. FDA approval of several immunotherapies has firmly established the role of this modality in the fight against cancer. A few of the leading immunotherapies include ICIs and adoptive cell therapy, or ACT.

Immune Checkpoint Inhibitors

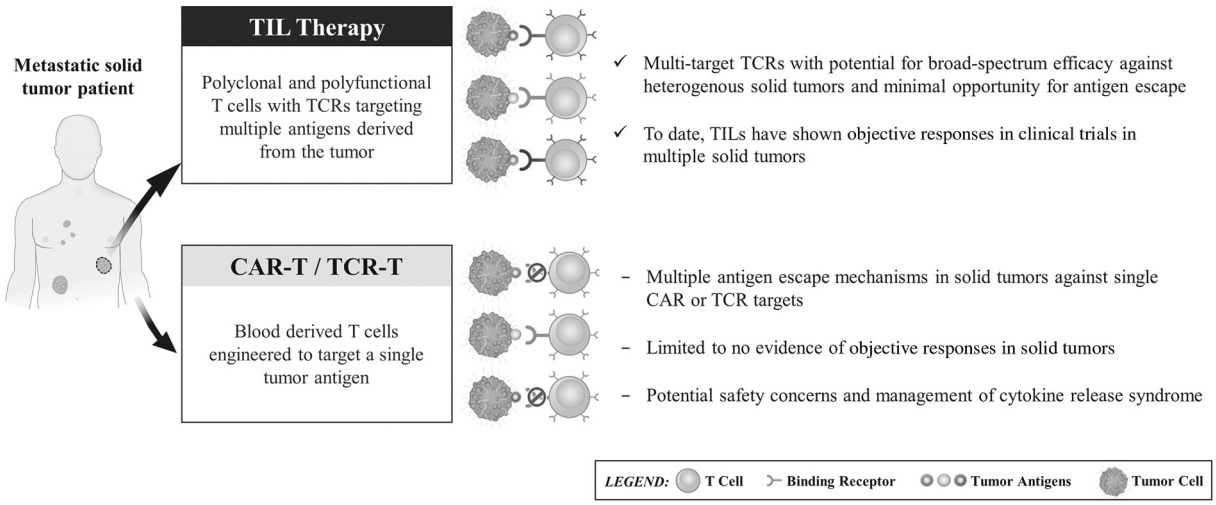
The development of ICIs represented a breakthrough for the treatment of various cancers. Immune checkpoints act as gatekeepers of immune responses, down-regulating T cell activity to prevent the destruction of healthy cells. However, cancer cells can also express these checkpoints to evade the immune system. Immune checkpoints have become the focus of numerous therapies that seek to block the activation of inhibitory immunoreceptors and reinvigorate antitumor function of immune cells. Monoclonal antibodies targeting immune checkpoints such as CTLA-4, PD-(L)1, and LAG-3 can restore antitumor immunity, thus reversing immune evasion and promoting tumor cell death. These therapies have found robust commercial success, with approximately $40.0 billion in worldwide sales in 2022. However, they have only incrementally improved broader patient outcomes, with less than 15% of all cancer patients responding to ICI therapy. The effectiveness of ICIs is heavily dependent on the presence of tumor-reactive T cells for this treatment to reinvigorate, and many patients lack enough T cells that recognize the target tumor. Furthermore, ICIs can promote systemic activation of self-reactive T cells resulting in immune-related adverse events.

Adoptive Cell Therapies

ACTs are immunotherapies that directly harness immune cells as the therapeutic modality. These immune cells, often T cells, are isolated from the patient or healthy donors, expanded, and sometimes engineered *ex vivo*, and then transferred into the patient. These processes allow for the expansion of T cells away from the immunosuppressive nature of the tumor microenvironment. While checkpoint inhibitors seek to re-activate the endogenous immune response, ACTs introduce immune cells into the body to attack target cancer cells. Most of the activity in ACTs has focused on ways to provide the requisite specificity of the T cells to cancer: identifying tumor-associated targets, evaluating their frequency on cancers versus healthy tissues, and evaluating the best ways to traffic T cells to them and attack the cancer. Three of the key ACT modalities utilizing T cells, that have been evaluated for the treatment of cancer include CAR-T, TCR-T, and TILs.

- *CAR-T*: CAR-T therapies are T cells extracted from blood that have been genetically engineered to express artificial cell surface receptors known as chimeric antigen receptors, or CARs. CARs are comprised of an extracellular binding domain specific to a surface molecule on tumor cells and an intracellular activation domain that turns the T cells "on" to kill tumor cells when the CAR binds to the tumor cell target. While patient-derived, or autologous, CAR-T therapies have been approved and have demonstrated responses in hematological cancers, they have resulted in significant off-tumor effects and limited to no objective responses in clinical trials in solid tumors. CAR-T therapies face a number of challenges in solid tumor settings, including lack of cell surface molecules that can be safely targeted, an inability to recognize intracellular tumor-specific proteins, and tumor antigen heterogeneity. Furthermore, the potent immune activation responsible for the success of CAR-Ts also drives the potential for life-threatening toxicity of cytokine release syndrome.
- *TCR-T*: TCR-T therapies are T cells extracted from blood that have been genetically engineered to express T cell receptors, or TCRs, that bind specific fragments of proteins presented by the human leukocyte antigen, or HLA, complexes on the surface of target cells. TCR-T therapies are engineered with a cloned TCR that directs the T cells to recognize peptides that arise from the tumor's mutated proteins or an aberrant or overexpressed self-protein. Unlike CAR-T therapies, TCR-T therapies have the potential to target intracellular proteins preferentially expressed by cancer cells. While there has been some limited clinical success in solid tumors, the HLA-dependent mechanism of TCR-Ts requires careful tissue matching between the transgenic TCR and the patient or the expression of engineered TCRs in the patient's own cells, thus restricting the addressable patient population. In addition, the targeted antigen may not be expressed uniformly across the tumor cells, and this heterogeneity can lead to ineffective targeting of the tumor, tumor escape and treatment-resistant tumor growth.
- *TILs:* TIL therapies are a type of ACT whereby lymphocytes including T cells are extracted from the patient's tumor, expanded outside the body, and then infused back into the patient. TILs contain T cells with a diverse set of TCRs and are polyclonal, meaning they recognize multiple different antigens, and polyfunctional, meaning that they have multiple effector functions. Due to these features, TILs have the potential to penetrate tumors and recognize and kill cancer cells and offer potential as a therapeutic for the treatment of solid tumors. To date, TILs have shown objective responses in clinical trials in solid tumors.

We believe that TILs have the potential to address the challenges of solid tumor recognition and heterogeneity in ways that CAR-Ts and TCR-Ts cannot, as illustrated in the figure below.



Responses Observed with Bulk TILs in Clinical Trials

Patient-specific TIL-based investigational therapies have been studied and developed for the treatment of solid tumors for over three decades. Pioneering work led by Dr. Steven A. Rosenberg, M.D., Ph.D., at NCI, first demonstrated objective responses in clinical trials of TILs in the treatment of melanoma. Most of the early work in TILs was focused on the development of an ACT using "bulk TILs," whereby all TILs extracted from a patient's tumor are isolated, expanded *ex vivo* and then reinfused into the patient.

Over the years, several hundred patients in the United States have received bulk TIL therapies across academia and industry sponsored clinical studies. In metastatic melanoma patients refractory to PD-(L)1 treatments, bulk TIL monotherapy has yielded objective response rates, or ORR, of approximately 30% to 50%, with complete response rates, or CRs, ranging from approximately 5% up to 20%. If a complete response lasts the lifespan of a patient, it would be considered as a cure – in general clinical practice patients are referred to as "cured" if they remain in complete response for greater than five years as the probability of their disease recurrence is low. Beyond metastatic melanoma, bulk TIL therapy has demonstrated early therapeutic potential in a limited number of solid tumors including squamous cell carcinoma of the head and neck, cervical cancer, and non-small cell lung cancer. To date, clinical trials of bulk TIL products have trended toward achieving their greatest success in cancers with a high number of mutations, also typically referred to as high tumor mutational burden, or TMB.

Limitations of Bulk TILs

The body of data spanning decades of research and clinical development in TILs has shed light on what we believe is the key feature that has made TILs successful to date, and also what has limited the success of bulk TILs to a subset of high TMB solid tumor indications. The therapeutic potential in any TIL product is driven by the "tumor-reactive T cells" that are characterized by recognition of tumor-specific antigens. Tumor-reactive T cells are polyclonal and polyfunctional populations of cells that can comprehensively recognize and kill a diverse population of heterogenous tumor cells unique to each patient.

We believe the key limitation of bulk TILs is the small subset of tumor-reactive T cells that exist in most bulk TIL products. Bulk TILs are routinely dosed at 10^9 cells or more, with tumor-reactive T cells representing reported median values of less than 3% *(Lowery et al., 2022)* of the total number of cells infused back into the patient. The tumor-reactive T cells included in bulk TIL products may be sufficient to drive utility in some patients with high TMB tumors. However, the fewer the number of mutations in the initial tumor material used to generate the bulk TIL product, the lower the number and proportion of tumor-reactive T cells included in a bulk TIL product, and consequently the lower the activity observed. In fact, across more than 50 patients with epithelial malignancies and low TMB tumors studied at the National Cancer Institute, or NCI, bulk TILs have demonstrated limited to no objective responses in clinical trials.

We believe the limitations described above highlight the need for the next generation of TIL therapy to selectively expand the necessary population of tumor-reactive T cells to maximize the benefit of TILs across a greater breadth of solid tumors. We believe that a greater population of tumor-reactive T cells delivered to a patient in a TIL product can expand the potential utility of TILs, if approved, to multiple solid tumor types.

Our Solution: Selected TILs

We are developing next generation TIL therapies for the potential treatment of multiple solid tumors. At present, no therapies in clinical development for our chosen solid tumor indications have demonstrated consistent curative outcomes for patients. Our innovative Selected TIL approach focuses on selecting and expanding the most potent tumor-reactive T cells to overcome the limitations of bulk TILs. This approach is grounded in work conducted in academia that has demonstrated improved clinical responses for selected TILs in solid tumor types where bulk TILs have not shown objective responses in clinical trials. We are leveraging this work to establish a standardized manufacturing process for large scale production of our Selected TILs.

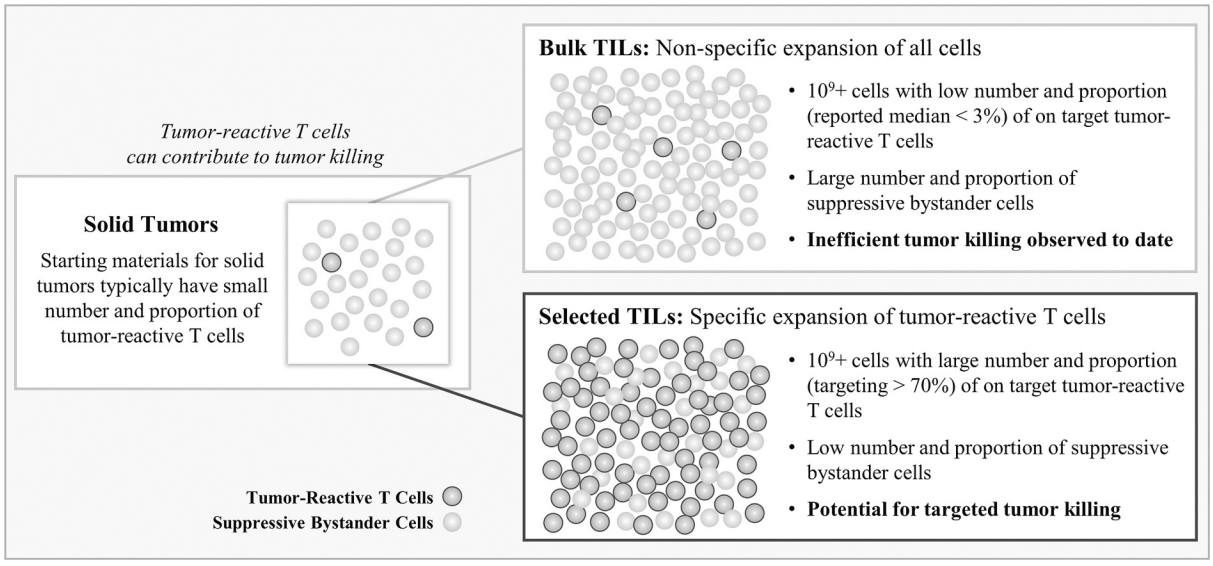
We are developing Selected TILs based on foundational principles with the goal of yielding the greatest number and proportion of tumor-reactive T cells in our TIL product candidates. We are developing TIL therapies for the potential treatment of a broad range of solid tumor types by employing the following principles:

(1) ***Unbiased identification of patient-specific tumor antigens****:* We seek to identify the most comprehensive set of patient-specific tumor antigens. We use an unbiased identification process that aims to find and capture the greatest diversity of antigens with the potential to drive the most robust T cell response, unlike other TIL products that are biased toward a specific subset or class of antigen(s), which may miss relevant tumor antigens or focus on the wrong targets.

(2) ***Selection of greatest breadth of tumor-reactive T cells from patient extracted TILs****:* Our goal is to capture and isolate the greatest number and proportion of a patient's tumor-reactive T cells that have the potential to attack and destroy heterogeneous solid tumors. We aim to select the greatest diversity of T cells, by using a functional-based screening process that confirms reactivity to the identified patient-specific tumor antigens rather than relying on a bioinformatics-based prediction algorithm that may not be truly predictive. Importantly, we seek to select for both CD8+ T cells, which can directly kill tumor cells, and CD4+ T cells, which stimulate and recruit other immune cells to tumor sites; studies have shown that the presence of both types of T cells is important for effective tumor control.

(3) ***Expansion of all tumor-reactive T cells and removal of all non-tumor-reactive bystander cells****:* We expand our selected tumor-reactive TIL population to magnitudes consistent with bulk TIL products and actively remove unnecessary bystander cells. This selective expansion has resulted in a substantially higher proportion of tumor-reactive T cells in the final product in comparison to the relatively infrequent tumor-reactive T cells that are routinely found in bulk TIL. Based on our non-clinical studies across multiple tumor samples to date, we have been able to achieve tumor-reactive T cell frequencies in our selected TIL drug product of up to 62%, with a median frequency of 23%. With ongoing continuous process improvements as part of our manufacturing strategy we are targeting >70% tumor-reactive T cells in our drug product as we advance clinical development.

The potential advantages of Selected TILs over bulk TILs are depicted in the figure below.

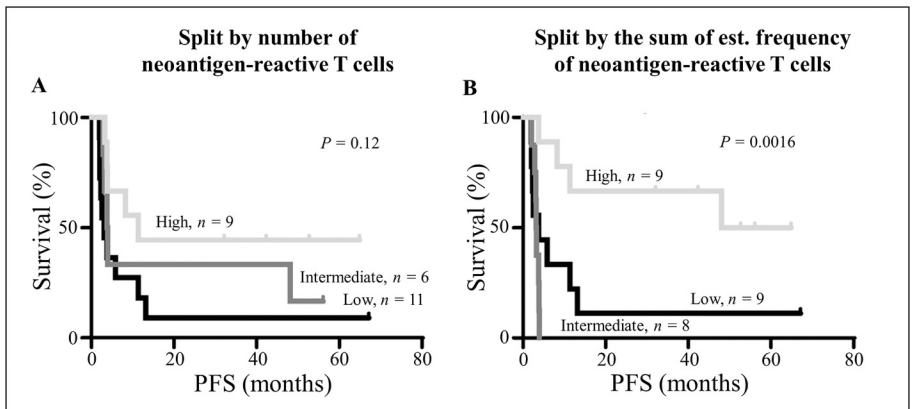


The approach described above is inherently designed to select for and characterize the active TIL product, *i.e.,* the tumor-reactive T cells. Bulk TIL approaches do not select for the active TIL product and have consequently faced challenges in product characterization and potency assay development. We believe that our Selected TIL approach will facilitate the development of potency release assays to support regulatory requirements and avoid the characterization challenges of bulk TILs.

Supporting Clinical Evidence

We believe the growing body of prospective and translational clinical data in the TIL field supports the potential of our Selected TIL approach.

A study by Kristensen *et al.* in 2022 reviewed data from 26 metastatic melanoma patients who were treated with TILs and evaluated the correlation between the number and frequency of tumor-reactive T cells in the TIL product and the level of progression-free survival, or PFS, observed. Progression-free survival is the length of time during and after the treatment of the patient's cancer, that a patient lives with their cancer but it does not get worse. PFS does not indicate that a patient is cured of their disease. As demonstrated in the figure below, patients that received TIL products with a high frequency of tumor-reactive T cells, more specifically referenced as neoantigen-reactive T cells in this study, experienced longer periods of PFS. Comparatively, patients receiving TIL products virtually devoid of tumor-reactive antigen recognition experienced rapid disease progression following TIL treatment.



PFS for the cohort splits by high (>66th percentile), intermediate (>33rd percentile), and low groups (≤ 33rd percentile). Neoantigen-reactive T cell (NARTs). (**A**) NART number 66th percentile = 5.65 NARTs. 33rd percentile = 0.88 (**B**) NART frequency. 66th percentile = 3.26%. 33rd percentile = 0.03%.

The key challenge for bulk TILs is that there is a limited number and breadth of these tumor-reactive T cells, which constrains the potential for bulk TILs to drive higher objective response rates in patients (vs. the objective response rates that have been observed in clinical trials to date). As a result, academic researchers have explored the potential of selecting or enriching for tumor-reactive T cells within the bulk TILs as a potential therapy for cancers where bulk TILs have not shown high objective response rates in clinical trials, including lung, breast, colorectal, and bile duct cancers.

Early academic selection and enrichment strategies typically utilized fragment-based selection and expansion approaches. Following harvest and dissection of the tumor, small numbers of tumor fragments were placed into separate multi-well tissue culture dishes and cultured with the tumor or manufactured antigens. TIL populations that were activated by exposure to tumor antigens in culture would then be identified based on cytokine expression and/or T cell activation marker expression, and only those activated TIL populations would be expanded for use in the final product.

A variation of this TIL selection approach demonstrated preliminary outcomes in non-small cell lung cancer in a study reported by Creelan *et al.* in 2021. Approximately 54% of the patients evaluable for clinical response in this study received TILs with confirmed tumor-reactivity, whereas the remainder received TIL products with no confirmed tumor-reactive T cells, which we believe demonstrates the crude and inconsistent nature of the academic manufacturing process. However, of the patients that received a TIL product with tumor-reactive T cells, 43% experienced a partial response, or PR, or CR, whereas all of the patients that received TILs without confirmed tumor-reactive T cells experienced disease progression, as shown in the table below. We believe this study

highlights the potential of selected TILs to generate positive outcomes in a challenging tumor indication, even with a rudimentary selection process.

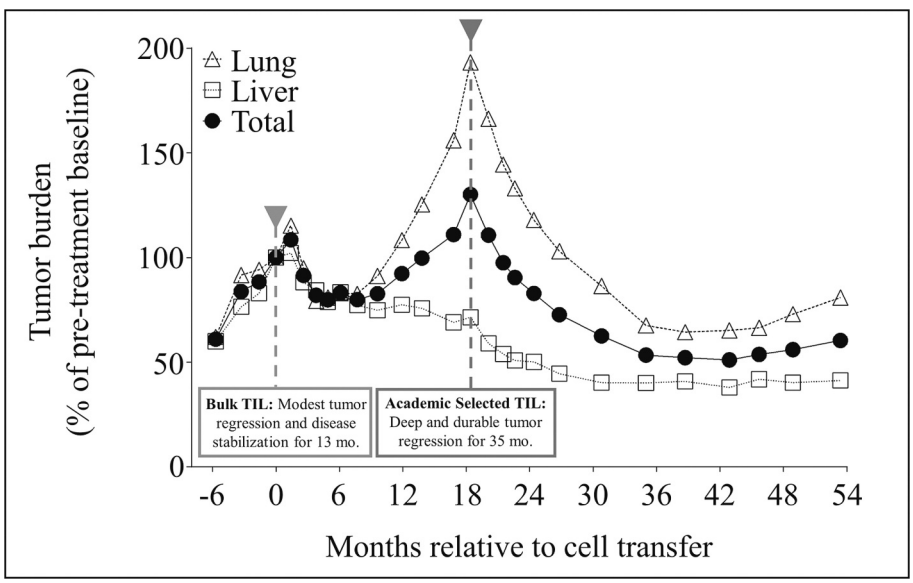
	Patients that received a TIL product ***with confirmed*** tumor-specific reactivity	Patients that received a TIL product ***with no confirmed*** tumor-specific reactivity
N*	7 (54%)	6 (46%)
N with confirmed ORR (%)	3 of 7 (43%)	0 of 6 (0%)
N with confirmed CR (%)	2 of 7 (29%)	0 of 6 (0%)

**only includes patients evaluable for clinical response (N=13)*

In clinical trials, TIL products enriched for tumor-reactive T cells using early selection strategies have also led to cancer regressions in difficult to treat epithelial malignancies including metastatic breast cancer, or mBrCa. Zacharakis *et al.,* in 2022 demonstrated that these TILs mediate regression in patients with breast cancer refractory to standard treatments. Three of six patients with mBrCa treated with infusion of tumor-reactive TILs developed objective cancer regression, and one CR was observed to be durable for more than 5.5 years.

This trial also highlighted the importance of different T cell populations in the TIL product. CD4+ T cells appeared to be the predominant population in the mBrCa TILs that demonstrated tumor reactivity. We believe this result suggests that successful selection strategies should include both CD8+ and CD4+ cells in the final TIL product.

Additional single patient academic studies in colorectal cancer in 2016 and bile duct cancer in 2014 conducted by Tran *et al.* utilizing early TIL selection strategies also have yielded responses. Notably, the bile duct patient was originally treated with bulk TILs that initially resulted in some tumor reduction, although the patient subsequently progressed. This patient was further treated with selected TILs at a point when the patient had higher disease burden and demonstrated a tumor regression that was durable for 35 months as shown in the graphic below.



The selection processes of the studies above differ from our Selected TIL approach due to a crude enrichment of tumor-reactive T cells through small pools of tumor fragments. These processes only partially enriched the drug products for tumor-reactive T cells and allowed carry over of bystander cells into the drug products. In contrast, our method of physical single cell sorting is designed to ensure selection of all tumor-specific antigen-reactive T cells and also facilitates efficient removal of bystander cells.

Building a Product Pipeline to Further Enhance the Quality and Function of Selected TILs

We believe our Selected TIL approach sets us apart from others in the industry that are utilizing bulk TILs, including newer bulk TIL approaches that introduce gene edits and culture media additives to enhance TIL quality and function. We believe that without the optimal starting population of tumor-reactive T cells, further enhancements or modifications to bulk TILs are unlikely to succeed in extending their potential utility beyond the limited tumor types where bulk TILs have already shown objective responses in clinical trials. We are also extending our product pipeline by making additional modifications to our proprietary Selected TILs and deploying them in differentiated combination strategies to further enhance TIL quality and function.

Modifications to Enhance TIL Quality

We are developing pipeline programs where we are evaluating enhanced culture conditions during the TIL production process to maintain and further improve TIL quality *ex vivo*. These enhanced culture conditions are designed to incorporate a mix of cytokines with the potential to rejuvenate dysfunctional and/or exhausted T cells.

Additionally, we plan to introduce functional genetic modifications into our pipeline programs that may drive potential for more sustained TIL quality and persistence *in vivo*. These gene edits will be designed to modify the tumor-reactive T cells to proliferate while resisting exhaustion post infusion, minimize their dependance on exogenous IL-2 for *in vivo* proliferation, and maintain their potential to kill tumors in suppressive tumor microenvironments. We are currently evaluating and prioritizing clinically informed targets for these genetic modifications.

Virus Combinations

Viral immunotherapy is a therapeutic modality with widespread potential to drive and modulate immune responses to tumors. The potential of viral immunotherapy has been validated by the FDA-approval of Talimogene laherparepvec for the treatment of metastatic melanoma. Many viruses have inherent oncolytic activity that can be modulated through genetic engineering. These viruses are characterized by the unique features of preferentially infecting, replicating within, and killing malignant tumor cells, as well as activating the immune response. Viral immunotherapies are designed to convert immunologically unresponsive "cold" tumor microenvironments to more reactive "hot" tumor microenvironments and thereby enhance the activity of immunotherapies including ICIs and ACTs, such as TIL therapies.

We believe we are strongly positioned to combine our Selected TIL product candidates with our proprietary viral immunotherapies utilizing two distinct approaches:

- *Viral immunotherapy pre-treatment (prior to TIL extraction) to optimize TIL harvest and broaden access to indications less amenable to TIL therapy*: Pre-treating the patient with a viral immunotherapy has the potential to disrupt the tumor and expose new antigens to the immune system thus driving a larger and more diverse population of tumor-reactive T cells. In addition, viruses elicit systemic cytokine production that can traffic T cells to the site of the tumor. We believe treatment with our viral immunotherapies could enable a superior TIL harvest, in quality, quantity and breadth of TILs. We plan to target this approach specifically to patients and indications for which the TIL yield is typically low, often leading to failure in generating sufficient TIL therapy for the patient.
- *Viral immunotherapy post-treatment (following delivery of the TIL product) to optimize TIL trafficking and function to further increase the activity of our TIL therapies*: Viral immunotherapy utilizes multi-mechanistic approaches to reprogram the immunosuppressive tumor microenvironment (*i.e.,* turn a "cold" tumor "hot") that can potentiate TIL infiltration, function, and proliferation within the tumor. In addition, virus at the tumor site is designed to serve as a beacon to call TILs to the site of the tumor. We believe treating the patient with viral immunotherapy following TIL infusion into the patient has the potential to further increase the activity of our TIL therapies, if approved, across several challenging solid tumors.

Our Pipeline

We are applying our Selected TIL approach for the potential treatment of a wide range of solid tumors. We are developing a broad pipeline aimed at improving outcomes for patients with cancers, as illustrated in the chart below.

Programs		Product Overview	Key Indications	Preclinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestone
Selected TILs	TIDAL-01	Tumor-reactive Selected TILs	Breast cancer; CRC; HNSCC; Uveal melanoma					Initial clinical data in mid-2024
			CRC; Cutaneous and non-cutaneous melanomas; HNSCC	Moffitt Collaboration*				
		Combination with viral immunotherapy	Solid tumors					IND submission
	TIDAL-02	Selected TILs with next-gen manufacturing and TIL quality enhancements	Solid tumors					IND submission

* Two concurrent investigator sponsored trials at Moffitt Cancer Center

CRC - Colorectal cancer; HNSCC - Head and neck squamous cell carcinoma

- ***TIDAL-01****:* Our lead Selected TIL product candidate utilizes an unbiased identification and functional screening process to isolate and selectively expand the greatest breadth of tumor-reactive T cells extracted from the patient's tumor. We have three ongoing Phase 1 clinical trials for TIDAL-01, including a multi-site trial for the treatment of breast cancer, colorectal cancer, head and neck cancer, and uveal melanoma, and two investigator sponsored trials with Moffitt, across colorectal cancer, head and neck cancer, and both cutaneous and non-cutaneous melanomas.

  Investigator sponsored trials are clinical trials where the investigator of the trial is also the "sponsor" of the trial for regulatory purposes. An "investigator" conducts clinical investigations and is the person under whose immediate direction the study drug is administered or dispensed to patients. A "sponsor" initiates and takes responsibility for a clinical investigation. A person who both initiates and conducts a clinical trial, and is responsible for all regulatory requirements, is designated as a "sponsor-investigator" by the FDA. Clinical investigators at academic medical centers who initiate clinical trials with a lawfully marketed drug to be used in a patient population or indication not within the official labeling often fit within this designation. In addition, as is the case with our investigator-sponsored trials, a company may provide a sponsor-investigator with supply of its unapproved product candidate and funding for the trial. Investigators who initiate and conduct such trials are responsible for obtaining an IND from the FDA and for ensuring compliance with the IND and associated regulatory requirements. As provided by the FDA's regulations, the sponsor of a clinical trial is responsible for, among other things, selecting qualified investigators, providing them with the information they need to conduct the trial properly, ensuring proper monitoring of the trial, ensuring that the trial is conducted in accordance with the protocols contained in the IND, maintaining an effective IND with respect to the trial, and ensuring that the FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug. In contrast, in a company-sponsored trial, the pharmaceutical company whose drug will be studied is the sponsor of the trial and, as such, is responsible for ensuring compliance with all regulatory requirements, including obtaining the IND.

  Under our multi-site trial, we control all aspects of our trial including, but not limited to, study protocol development, patient selection and enrollment, regulatory interactions, data release, and manufacturing through our industrial contract development and manufacturing organization, or CDMO. Under the investigator sponsored trial, which is fully funded by us, Moffitt is solely responsible for regulatory interactions, trial conduct and manufacture of TIDAL-01 at the Moffitt Cancer Cell Therapy Facility, with input and support from us at Moffitt's discretion. Investigators at Moffitt are also solely

responsible for the design of the trial and patient selection and enrollment, where we remain in close contact with the investigators to provide our input if appropriate. Any data disclosures will be made in collaboration with us and any improvements to the TIDAL-01 manufacturing process are solely at our discretion. We intend to provide an initial clinical update across these two trials in mid-2024.

- ***TIDAL-02****:* Our next generation Selected TIL program encompasses a streamlined manufacturing process designed for selecting tumor-reactive T cells, with additional modifications to enhance TIL quality and function. TIDAL-02 is currently in preclinical development.
- ***Selected TIL and viral immunotherapy****:* Our combination strategies are designed to improve TIL harvest and overcome the immunosuppressive tumor microenvironment for better trafficking and expansion of TILs *in vivo.* We are currently evaluating the optimal viral immunotherapy for combination with TIDAL-01 to advance into clinical development.

TIDAL-01

Overview

TIDAL-01 is our lead Selected TIL product candidate that we are advancing in multiple solid tumor indications. TIDAL-01 utilizes an unbiased identification and functional screening process to isolate and selectively expand the most comprehensive set of tumor-reactive TILs from the patient's tumor. Our TIDAL-01 production process is designed to deliver at least 10^9 cells and targets greater than 70% functional and potent tumor-reactive T cells.

We have a multi-site Phase 1b clinical trial ongoing for TIDAL-01 in patients with solid tumors such as breast cancer, colorectal cancer, head and neck cancer, and uveal melanoma, which are indications where bulk TILs have not historically shown objective and/or durable responses in clinical trials. Additionally, our two ongoing investigator sponsored Phase 1 clinical trials in collaboration with Moffitt will evaluate TIDAL-01 in colorectal cancer, head and neck cancer, and multiple types of melanoma including cutaneous melanomas, an indication where bulk TILs have shown objective responses in clinical trials. We are very early in our development efforts, and as we make progress, if we obtain positive results of sufficient magnitude from one or both trials, we intend to discuss, receive guidance and the appropriate acceptance from the relevant regulatory agency(ies) to determine if we will be advancing TIDAL-01 into pivotal trials, which are trials that are intended to secure regulatory approval for a product candidate. We plan to provide an initial clinical update on the TIDAL-01 program in mid-2024.

Background on Breast Cancer, Colorectal Cancer, Head and Neck Cancer, Uveal Melanoma, and Cutaneous Melanoma

Breast cancer: Breast cancer makes up approximately 15% and 14% of all new cancer cases in the United States and Europe, respectively. About one in eight U.S. women and one in 11 European women will develop invasive breast cancer over the course of her lifetime. In 2024, an estimated 314,000 new cases and 43,000 deaths are projected to occur in the United States. In the European Union, approximately 379,000 people were estimated to have been diagnosed with breast cancer in 2022, along with an estimated 97,000 deaths. Nearly 30% of women diagnosed with early-stage breast cancer will eventually develop metastatic disease. Breast cancer is the second leading cause of cancer death in women in the United States, only trailing lung cancer. In recent years, improvements in early diagnosis and treatment have improved survival rates by approximately 1% per year, but the five-year survival rate for women with metastatic breast cancer is 28%. Treatment options and recommendations depend on several factors, including the tumor's subtype, stage, genomic markers, the patient's age, and presence of known mutations in inherited breast cancer genes, but may include surgery, radiation therapy, chemotherapy, hormonal therapy, targeted therapy, and immunotherapy.

Colorectal cancer, or CRC: CRC is the third most commonly diagnosed cancer and ranks second in terms of mortality in the United States. In 2024 in the United States, it is estimated that there will be approximately 153,000 new CRC cases, and 53,000 deaths. In the European Union, approximately 356,000 people were estimated to have been diagnosed with CRC in 2020, and there were approximately 159,000 deaths. Of these cases, approximately 85% of patients are characterized as microsatellite stable, or MSS as opposed to the approximately 15% which are microsatellite instable, or MSI. Whereas the microsatellite instability-high, or MSI-H, phenotype confers good

prognosis and greater response to immunotherapy in CRC, MSS tumors are generally considered 'cold' tumors and are less responsive to immunotherapies, with anti-PD-(L)1 therapy demonstrating nearly no effect. The five-year survival rate for all colorectal cancer in the United States is approximately 65% and drops below 20% if the cancer has metastasized. Treatment options for CRC include surgery, radiation therapy, chemotherapy, targeted therapy, and immunotherapy.

Head and Neck Squamous Cell Carcinoma, or HNSCC: HNSCC accounts for approximately 90% of all head and neck cancers and is the seventh most common cancer worldwide, with 890,000 new cases and 450,000 deaths annually. The overall incidence of HNC continues to rise, with a predicted 30% increase annually by 2030. The number of new cases of HNSCC in the United States in 2024 is expected to be 64,000, with 15,000 expected deaths. There were approximate 120,000 new cases of HNSCC in Europe in 2022, and an estimated 63,000 deaths. HNSCC comprises a group of malignancies mostly derived from the mucosal epithelium in the oral cavity, pharynx and larynx. Oral cavity and larynx cancers are generally associated with tobacco consumption, alcohol abuse or both, whereas pharynx cancers can be attributed to infection with human papillomavirus (HPV). The treatment approach for oral cavity cancers generally consists of surgery followed by chemotherapy plus radiation (CRT) while pharynx and larynx cancers are primarily treated with CRT. For the treatment of recurrent and unresectable disease, immune checkpoint inhibitors, including pembrolizumab and nivolumab, have been approved as primary treatment. Approximately 30% to 40% of patients present with early-stage disease, and the five-year overall survival in these patients is 70% to 90%, which is reduced to approximately 39% for patients with metastatic HNSCC. Patients with recurrent disease have a poor prognosis, though those with only locoregionally recurrent disease may benefit from definitive treatment. The toxicity associated with current treatment regimens is substantial.

Uveal melanoma: Uveal melanoma is a rare and aggressive form of melanoma that affects the eye. It is the most common primary intraocular malignancy in adults, and represents approximately 85% of all ocular melanomas.. In the United States, it is estimated that there are approximately 5,000 new cases of uveal melanoma per annum, and approximately 3,000 in Europe. About 5% of patients present with metastatic disease, and up to 50% will eventually develop metastatic disease, usually involving the liver and less frequently lung, bone, and other organs. Epidemiology of uveal melanoma varies by region and ethnicity. Treatment generally involves surgery if metastases are not present and radiation therapy. In cases where uveal melanoma is constrained to the eye, five-year survival rates are about 85%, but if the disease spreads to other organs, the five-year survival rate is 13%. While there is one FDA-approved drug for the treatment of unresectable or metastatic uveal melanoma, there remains a medical need due to a number of factors including only a subset of patients being eligible for treatment by the approved product. Other potential treatment options include anti-PD-(L)1 or anti-CTLA-4 checkpoint inhibitors, chemotherapy, and kinase inhibitors.

Cutaneous melanoma: Cutaneous melanoma, or melanoma of the skin, is the most common form of melanoma. In the United States, approximately 101,000 new melanoma cases are expected to be diagnosed in 2024, and 8,000 deaths. Across Europe in 2022, there was an estimated 102,000 new cases, and 17,000 deaths. Melanoma is unique compared to non-melanoma skin cancers in that it tends to spread locally, regionally, and distantly. Metastatic spread risk is high in melanoma patients, with approximately 5% of melanoma cases being metastatic at diagnosis, and most often involves skin and subcutaneous tissues, lungs, liver, bones and brain. Surgery is the main treatment option for most melanomas and usually cures localized invasive melanoma. For melanomas that have metastasized to other areas of the body or organs that cannot be surgically removed, radiation, checkpoint inhibitor therapy (anti-PD-(L)1 with or without anti-CTLA-4), targeted therapy or chemotherapy are the most common treatment options, with a five-year survival rate of approximately 23%.

Our Solution: TIDAL-01

TIDAL-01 is a Selected TIL product candidate that utilizes an unbiased identification and functional screening process designed to isolate and selectively expand the greatest breadth of tumor-reactive TILs from the patient's tumor. We are developing TIDAL-01 for the potential treatment of a broad range of solid tumor types.

We have developed consistent and scalable current good manufacturing practice, or cGMP manufacturing for TIDAL-01 designed to deliver a potent tumor-reactive T cell product. The manufacture of each TIDAL-01 product is initiated by harvesting the patient's tumor samples through surgical resection and collecting monocytes from the

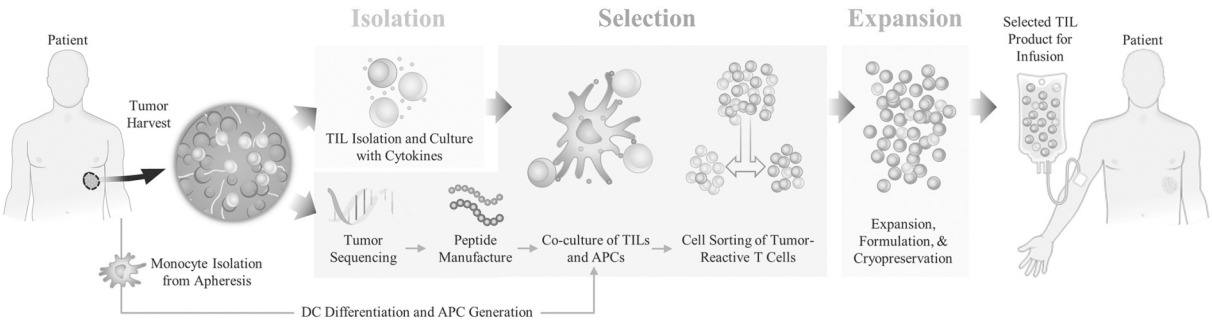
blood through apheresis. The three key processes steps to manufacture TIDAL-01 are isolation, selection, and expansion:

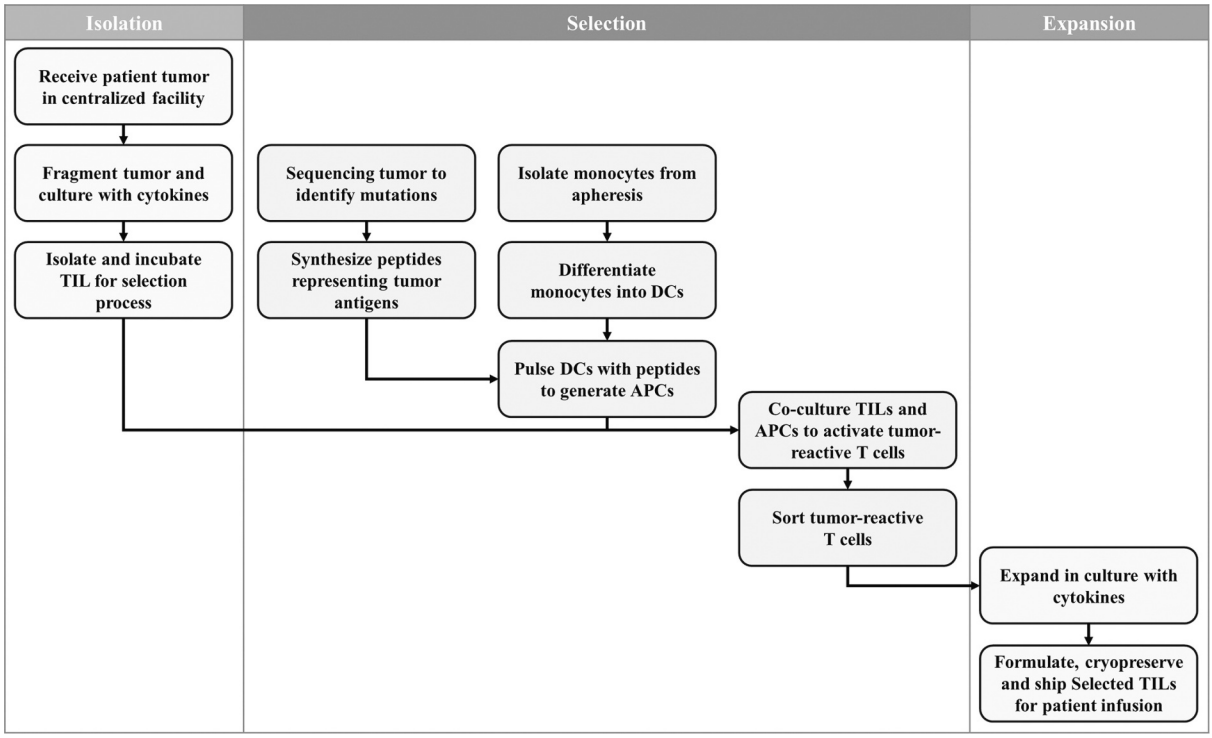
- *Isolation:* Tumor samples are shipped to a centralized manufacturing facility where the tumor is dissected into small fragments and cultured with cytokines. TILs are then isolated from the tumor fragments and incubated to generate a sufficient population of cells to perform the selection process.
- *Selection:* The patient's tumor sample is sequenced and mutations that are specific to the tumor are identified based on comparisons to the patient's healthy tissue. These mutant sequences are used to generate more than 190 unique peptides that represent potential tumor antigens. We believe that this number of peptides can cover the full set of tumor antigens found in low TMB tumors. In the case of high TMB tumors where more than 200 antigens have been identified, we use our in-house bioinformatics capabilities to prioritize the most immunogenic antigens for peptide generation.

  In parallel, monocytes from the apheresis product are differentiated into dendritic cells, or DCs. The synthesized peptides are incubated with the DCs, which process and present the antigens to become antigen-presenting cells, or APCs.

  In order to identify tumor-reactive T cells within the isolated TILs, we utilize a functional screening process leveraging these APCs. The isolated TILs are co-cultured with APCs and only the tumor-reactive T cells that recognize the antigens on the APCs become activated. These activated tumor-reactive T cells are then physically sorted from the cells that are not tumor-reactive on the basis of well-established activation markers. This process is designed to generate Selected TILs that capture the greatest breadth of tumor-reactive T cells and remove potentially detrimental bystander cells.
- *Expansion:* These Selected TILs are expanded in culture with cytokines to a target of 10^9 or more cells, which we believe represent a therapeutically relevant dose. The cells are then formulated, cryopreserved, and shipped to the clinical site for patient administration.

  These three processes steps are depicted in the schematic and associated process flow chart below:





Our process is designed to result in a Selected TIL therapy targeting at least 10^9 cells with the following product attributes:

- Targets greater than 70% tumor-reactive T cells
- Polyclonal and polyfunctional mix of CD4+ and CD8+ cells
- Potential to target a large breadth of antigens specific to each individual patient
- Potential to stimulate broad immunological responses
- Clearly defined potency parameters

Manufacturing, Process Development, and Analytical Characterization

To date, we have completed multiple manufacturing runs that meet clinical specifications to establish readiness for clinical manufacturing. All completed runs successfully demonstrated consistency and reproducibility of desired yield, distribution of CD8+ and CD4+ T cells, and anticipated preliminary potency parameters of the TIDAL-01 product at good current manufacturing practice, or cGMP scale.

Manufacturing of TIDAL-01, from the collection of patient samples to the infusion of the drug product into the patient, currently takes around eight weeks. We have ongoing in-house process development efforts focused on reducing manufacturing time to approximately four weeks by optimizing critical steps in manufacturing, supply chain and logistics. Some improvements include establishing in-house tumor sequencing capabilities, expediting synthesis and shipping of peptides and reducing the duration of the expansion process. Most of our efforts to reduce manufacturing time are well underway and we expect to have the key improvements fully implemented prior to the initiation of any pivotal trials.

Our TIDAL-01 process is inherently designed to select for and characterize the tumor-reactive T cells that provides the tools to measure tumor specific potency and facilitate the development of potency release assays to support regulatory requirements and avoid the characterization challenges of bulk TILs. We have implemented a comprehensive sample retention strategy for the final TIL product manufactured per patient as well as critical raw

materials and process intermediates to facilitate a robust analytical characterization program, with a variety of functional and phenotypic assays deployed for potency assessment.

TIDAL-01 is currently deployed at two primary manufacturers for the isolation, selection, and expansion steps: the Moffitt Cancer Center Cell Therapy Facility and an industrial contract development and manufacturing organization, or CDMO. We believe that continuing to maintain full control of our manufacturing network and supply chain, across our overall pipeline, is central to our success and a core component of our strategy. As TIDAL-01 progresses in clinical development, we expect to continue to form and expand strategic external partnerships across all facets of our manufacturing and supply chain. If we demonstrate clinical success of TIDAL-01, we intend to explore both the design, engineering, construction, commissioning, and operation of a fully integrated commercial manufacturing supply chain, as well as external strategic partnerships that are favorable to us and satisfy anticipated manufacturing demand.

Strategic Alliance and Collaboration with Moffitt Cancer Center

We have entered into a strategic alliance with Moffitt, an academic leader in the TIL field to leverage their expertise for advancement of TIDAL-01 into the clinic. Moffitt has significant experience in conducting cell therapy clinical trials, and specialized expertise in treating patients with TIL therapies. Moffitt has on-site cGMP facility for clinical manufacturing of TIL products and laboratories which provides them with research and translational support. We have partnered with Moffitt to open two TIDAL-01 INDs for investigator sponsored trials for the treatment of colorectal cancer, head and neck cancer, and both cutaneous and non-cutaneous melanomas. Under the strategic alliance, Moffitt will provide us support for clinical site activation and patient recruitment. Additionally, Moffitt will support the ongoing trial with dedicated cleanroom capacity and manufacturing priority at their on-site cGMP facility for TIDAL-01 production. In parallel, we are also working with Moffitt on our dedicated pre-clinical research studies supporting the use of our Selected TILs in solid tumor types, including breast and gastrointestinal cancers.

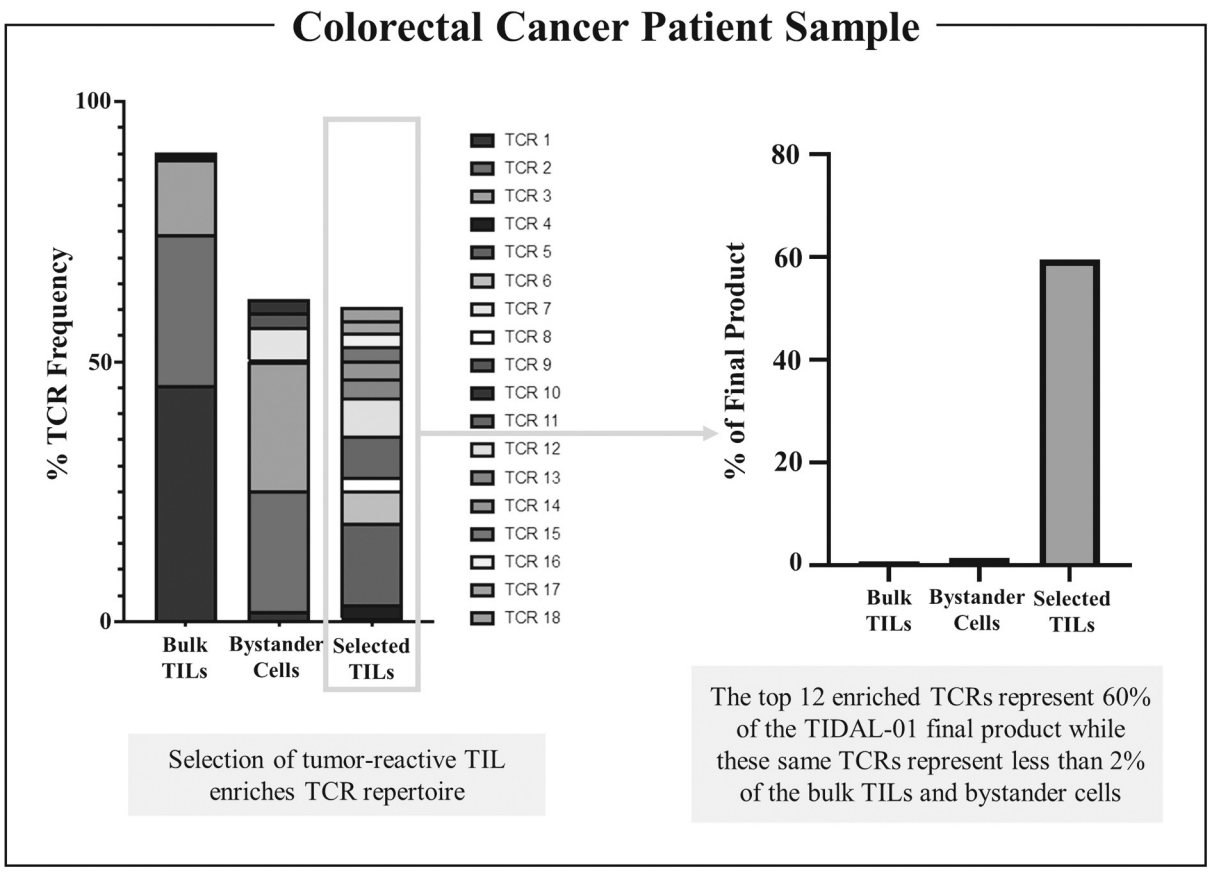
Nonclinical Studies

In order to evaluate the therapeutic potential of TIDAL-01, we conducted a series of nonclinical studies using Selected TILs generated with our TIDAL-01 process from patients with various solid tumor types. Substantial variability in our nonclinical study results were observed based upon heterogeneity of individual tumor samples, which can impact the magnitude of effects of the TIDAL-01 process. We provide sample data below that represents the directional effects of the TIDAL-01 process in each of these studies.

1. Consistent enrichment of tumor-reactive T cells targeting multiple relevant patient-specific tumor antigens

TIDAL-01 is designed to select for T cells that are specifically reactive to the patient's tumors. Using TILs generated from patients with multiple solid tumor types employing the TIDAL-01 process, we evaluated the T cell receptor, or TCR, repertoire of the TILs using next-generation sequencing before and after the selection step of our process. We then evaluated the frequency of T cells in the samples that recognized patient-specific tumor antigens. We consistently observed that Selected TILs displayed an enriched TCR repertoire and increased T-cell reactivity toward patient-specific tumor antigens relative to the bulk TIL comparator.

To further evaluate enrichment of tumor-reactive T cells, we compared the frequencies of TCRs in TIDAL-01 versus bulk TILs in 10 tumor samples. The data shown below has been generated from a colorectal cancer patient. The left side of the figure below shows the frequency of the top approximately 20 most abundant TCRs in the bulk TIL sample, the TIDAL-01 Selected TIL sample, and the non-tumor-reactive bystander cells removed during the TIDAL-01 Selection process. This study demonstrated that relatively few TCRs predominated in bulk TIL products, and that those abundant TCRs were non- tumor-reactive, as evidenced by overlap of the predominant TCRs in the bulk TIL with the bystander cell TCRs. Conversely, our Selected TILs displayed a more diverse and less biased TCR repertoire, which we anticipate will enable the Selected TILs to target a large breadth of patient-specific tumor antigens. The TIDAL-01 selection process enriched tumor-reactive T cells by approximately 30-fold in comparison to frequencies present in bulk TIL.



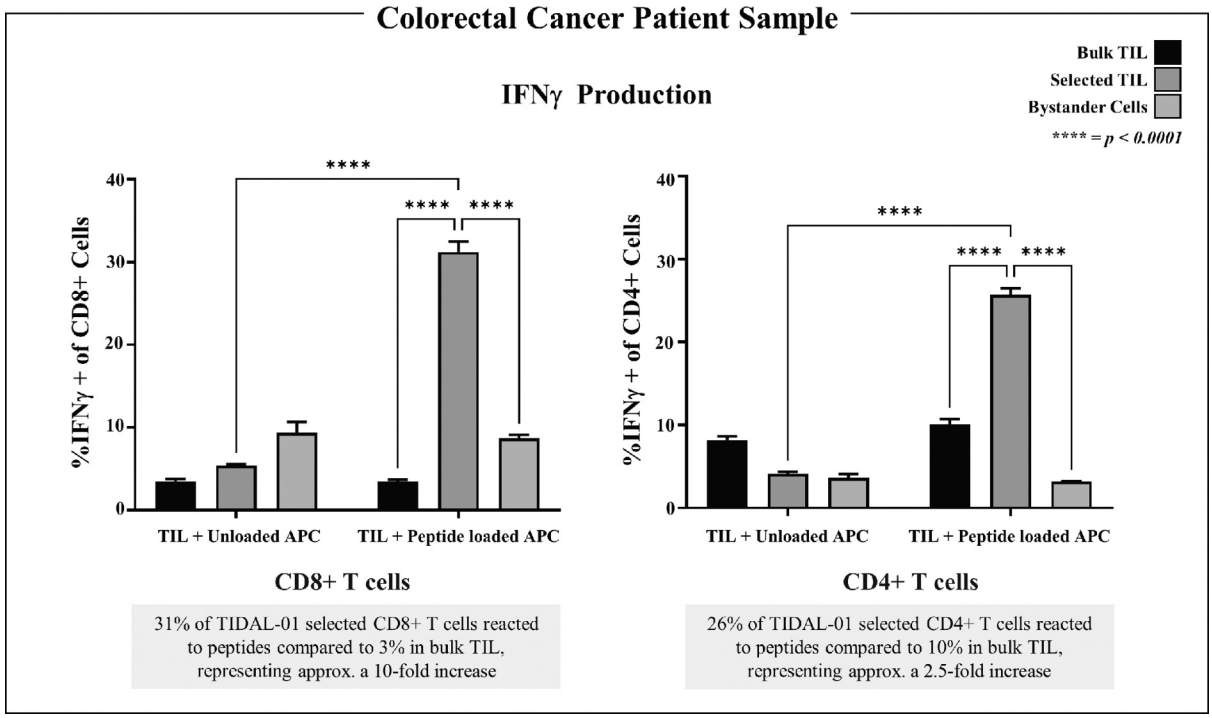
Across all the samples where we conducted this assessment, in comparison to frequencies present in bulk TIL, the TIDAL-01 process enriched tumor-reactive T cells by a range of 1.5 to 43-fold, with an average of approximately 11-fold increase.

2. Selection and enrichment of therapeutically relevant quantities of both CD4+ and CD8+ tumor-reactive T cells

In order to further evaluate the tumor-reactive T cell population in TIDAL-01, we conducted flow cytometry studies using Selected TILs and bulk TILs from the same colorectal cancer patient. The purpose of this study was to compare the percentage of tumor-reactive CD4+ and CD8+ T cells resulting from these processes.

Representative cytokine staining data is depicted in the figure below. The frequency of tumor-reactive T cells in each sample is depicted by the percentage of cells that express interferon gamma, or IFNγ, in response to tumor antigens presented by "peptide loaded APC". For the Selected TILs, bulk TILs, and bystander cells, we measured tumor-reactive CD4+ and CD8+ T cells after incubating the TIL samples with APCs displaying patient-specific

tumor antigens and with APCs without patient-specific tumor antigens. As shown below, Selected TILs generated by TIDAL-01 contained far higher frequencies of tumor-reactive CD4+ and CD8+ T cells relative to bulk TILs.

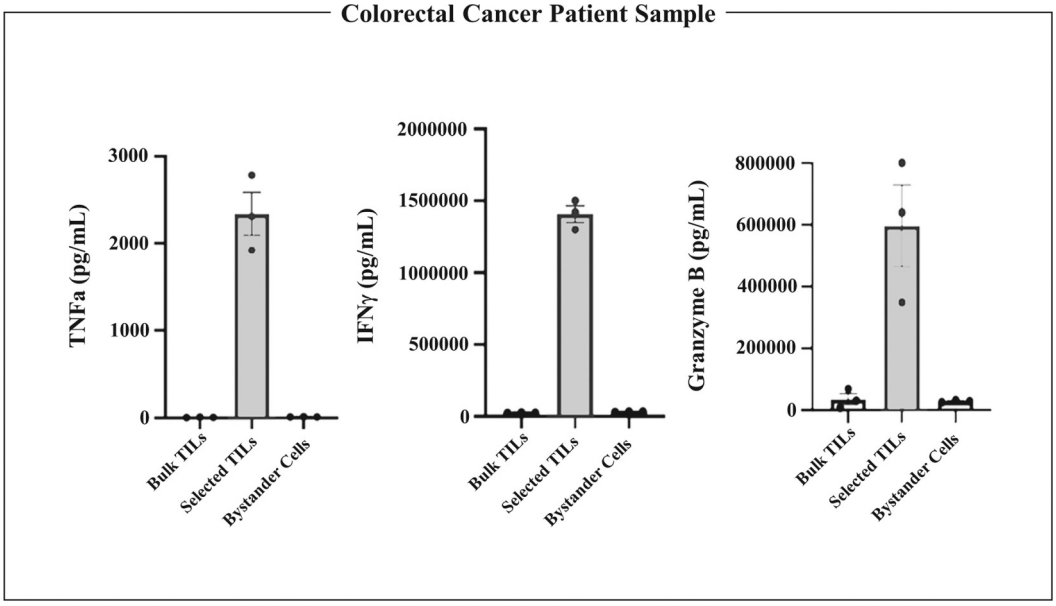


This study was conducted using Selected TILs and bulk TILs generated from 6 tumor samples, and the frequencies of tumor-reactive CD4+ and CD8+ T cells in Selected TILs relative to bulk TILs ranged from a 1.5 to an approximately 10-fold increase, with an average of approximately 3-fold increase for both cell types.

3. Polyfunctional anti-tumor activity of Selected TIL products

We compared the potency of Selected TILs and bulk TILs from the same patients across 13 solid tumor samples by measuring the expression of key indicators following exposure to patient-specific tumor antigens. The expression of IFNγ and tumor necrosis factor α, or TNFα, in response to patient-specific tumor antigens indicates the potential of TILs to orchestrate broad anti-tumor immunological responses, and the expression of granzyme B indicates the potential of TILs to kill nearby tumor cells. The figure below depicts results from a colorectal cancer patient comparing the expression of these potency indicators as measured by enzyme-linked immunosorbent assay for the bulk TILs, the TIDAL-01 Selected TILs, and the non-tumor-reactive bystander cells removed during the TIDAL-01 Selection process. The columns highlighted in blue indicate that our Selected TILs displayed several orders of magnitude higher levels of potency indicators when compared to bulk TILs or bystander cells for a

colorectal cancer patient sample. Additionally, the responses of bulk TIL resembled those of bystander cells, suggesting the predominance of bystander cells in the bulk TIL population.

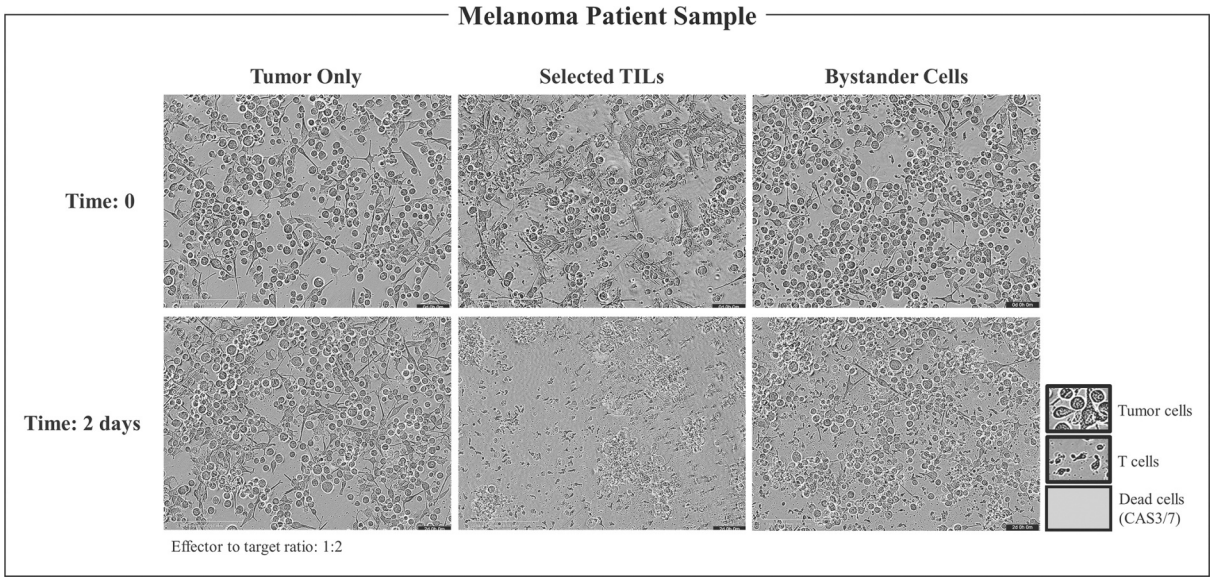


Across all the samples from which we conducted this assessment, for IFNγ, the fold increase between the TIDAL-01 Selected TILs and the bulk TILs ranged between 2 to 86-fold, with an average increase of approximately 27 fold; for TNFα the fold increase between the TIDAL-01 Selected TILs and the bulk TIL ranged between 1.6 to 95-fold with an average increase of approximately 25-fold; and for granzyme B the fold increase between the TIDAL-01 Selected TILs and the bulk TIL ranged between 1.5 to 33-fold with an average increase of approximately 9 fold.

4. Tumor-killing activity of Selected TIL products

In order to evaluate the antitumor activity of TIDAL-01, we compared the impact of Selected TILs and bystander cells from the same patient on tumor cells derived from that patient. Selected TILs and bystander cells were mixed with patient-derived tumor cells for 48 hours. The cell populations were analyzed by video microscopy, and image analysis algorithms were used to assess the number of dead and alive tumor cells at regular intervals. Selected TILs displayed a higher capacity to kill tumor cells relative to bystander cells as depicted in the figure below for a melanoma patient sample. Given the considerable technical challenges in maintaining patient-derived

tumors as disaggregated single cell cultures that maintain tumor-reactive antigen expression, we have completed this study only using the single melanoma patient sample depicted below.



5. Functionally competent T cells in the final product

To ensure that TIDAL-01 is comprised of functionally competent T cells, we conducted an immunophenotypic analysis of Selected TILs following the TIDAL-01 Expansion process. Multiparameter flow cytometry was used to quantify the expression of key indicators of functionality, including markers for T cell exhaustion (PD-1, TIM-3 and LAG-3) and T stem central memory, or Tscm (CD45RA+, CCR7+ and CD27+).

In a single sample that was assessed for overlapping expression of PD-1, TIM-3 and LAG-3, TIDAL-01 showed low (2%) and predominantly non-overlapping expression of PD-1, TIM-3 and LAG-3, indicating a lack of functional exhaustion in the final drug product. Additionally, in 3 tumor samples that were assessed for overlapping PD-1 and TIGIT expression representative of exhaustion, only 0.7% - 11% of the drug product demonstrated overlapping expression of the two markers.

In a single sample that was assessed, TIDAL-01 also demonstrated a relatively high frequency of cells co-expressing CD45RA+, CCR7+, and CD27+, indicating the presence of a Tscm subset. The frequency of long-lived T cells displaying markers associated with Tscm populations has been associated with enhanced outcomes in response to T cell immunotherapy (Ren, Cao & Wang 2021), and there is clinical evidence of a highly significant association between the likelihood of having a complete response and the infusion of TIL containing CD8+ CD27+ cells (Rosenberg et al., 2011).

Clinical Development Strategy

Our clinical strategy is designed to evaluate the activity of TIDAL-01 in multiple solid tumor indications. We seek to: (i) generate clinical data in indications where objective and/or durable responses for bulk TILs have not been demonstrated in clinical trials and (ii) determine the clinical activity of TIDAL-01 in indications where bulk TILs have previously shown objective response rates in clinical trials.

Multisite solid tumor clinical trial: We have an ongoing multicenter Phase 1 trial evaluating TIDAL-01 for the treatment of patients with breast cancer, colorectal cancer, head and neck cancer and uveal melanoma. These tumor types are generally characterized by a low TMB, and have not historically benefited from bulk TIL therapy. Given the limited treatment options in these indications, the historically low response rates, and our belief in the therapeutic potential of Selected TILs in challenging solid tumors, we are developing TIDAL-01 for the potential

treatment of these indications. We are initially targeting enrollment of 40 to 60 patients across the four indications with the following criteria:

- Patients with unresectable or metastatic breast cancer who have relapsed on at least one prior treatment for metastatic disease including guideline directed targeted therapy for eligible subtypes.
- Patients with unresectable or metastatic colorectal cancer including both MSS and MSI subtypes. MSS-colorectal cancer patients must have received a prior regimen containing at least oxaliplatin or irinotecan. MSI-colorectal cancer patients must have failed or progressed on a prior regimen with anti-PD-(L)1 therapy.
- Patients with unresectable or metastatic head and neck squamous cell carcinoma, excluding nasopharyngeal and nasal cavity carcinomas, who are PD-1/PD-L1 inhibitor naive and have received no prior therapy for metastatic disease.
- Patients with uveal melanoma that have only received local-regional or adjuvant therapy if systemic treatments are contra-indicated or unavailable.

Multi-indication clinical trials at Moffitt Cancer Center: We have two ongoing investigator sponsored Phase 1 clinical trials for TIDAL-01 in collaboration with Moffitt, Investigator sponsored trials are clinical trials where the investigator of the trial is also the "sponsor" of the trial for regulatory purposes. An "investigator" conducts clinical investigations and is the person under whose immediate direction the study drug is administered or dispensed to patients. A "sponsor" initiates and takes responsibility for a clinical investigation. A person who both initiates and conducts a clinical trial, and is responsible for all regulatory requirements, is designated as a "sponsor-investigator" by the FDA. Clinical investigators at academic medical centers who initiate clinical trials with a lawfully marketed drug to be used in a patient population or indication not within the official labeling often fit within this designation. In addition, as is the case with our investigator-sponsored trials, a company may provide a sponsor-investigator with supply of its unapproved product candidate and funding for the trial. Investigators who initiate and conduct such trials are responsible for obtaining an IND from the FDA and for ensuring compliance with the IND and associated regulatory requirements. As provided by the FDA's regulations, the sponsor of a clinical trial is responsible for, among other things, selecting qualified investigators, providing them with the information they need to conduct the trial properly, ensuring proper monitoring of the trial, ensuring that the trial is conducted in accordance with the protocols contained in the IND, maintaining an effective IND with respect to the trial, and ensuring that the FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug. In contrast, in a company-sponsored trial, the pharmaceutical company whose drug will be studied is the sponsor of the trial and, as such, is responsible for ensuring compliance with all regulatory requirements, including obtaining the IND.

Under our multi-site trial, we control all aspects of our trial including, but not limited to, study protocol development, patient selection and enrollment, regulatory interactions, data release, and manufacturing through our CDMO. Under the investigator sponsored trials, which are fully funded by us, Moffitt is solely responsible for regulatory interactions, trial conduct and manufacture of TIDAL-01 at the Moffitt Cancer Cell Therapy Facility, with input and support from us at Moffitt's discretion. Investigators at Moffitt are also solely responsible for the design of the trials and patient selection and enrollment, where we remain in close contact with the investigators to provide our input if appropriate. Any data disclosures will be made in collaboration with us and any improvements to the TIDAL-01 manufacturing process are solely at our discretion.

We have two active investigator sponsored phase 1 trials ongoing in collaboration with Moffitt. In this trial we are targeting enrollment of approximately 35 patients across four cohorts including:

- Patients with cutaneous (non-acral) melanoma having failed prior anti-PD-(L)1, anti-CTLA-4, and BRAF+/- MEK inhibitor if BRAF V600 mutant.
- Patients with acral, mucosal, or uveal melanoma having failed prior standard of care in the opinion of the investigator.
- Patients with melanoma (cutaneous, mucosal, or uveal) undergoing therapeutic resection whose tissue samples were collected and banked and who have a high likelihood of recurrence or progression within two years. TIDAL-01 product will only be generated and administered to these patients at time of recurrence.

- Patients with unresectable or metastatic colorectal cancer including both MSS and MSI subtypes. MSS-colorectal cancer patients must have received a prior regimen containing at least oxaliplatin or irinotecan. MSI-colorectal cancer patients must have failed or progressed on a prior regimen with anti-PD-(L)1 therapy.

In the second trial, we are targeting enrollment of approximately 15 patients in a single indication cohort:

- Patients with unresectable or metastatic head and neck squamous cell carcinoma, excluding nasopharyngeal and nasal cavity carcinomas, who are anti-PD-(L)1 inhibitor naive and have received no prior therapy for metastatic disease.

All patients across our trials will undergo surgery to remove a small amount of their tumor to initiate the manufacturing process. The patient-specific TIDAL-01 product candidate will be manufactured and sent back to the clinical site, and patients will be treated with a conditioning regimen that includes lymphodepleting chemotherapy prior to treatment with TIDAL-01 and treatment with IL-2 following TIDAL-01 infusion, to support further proliferation of TIDAL-01 *in vivo*. Both lymphodepleting chemotherapy and treatment with IL-2 are standard for bulk TIL therapies.

In our multi-site solid tumor trial, patients will also be receiving pembrolizumab as their anti-PD-(L)1 treatment two weeks after the TIDAL-01 infusion. Combination with anti-PD-(L)1 has the potential to enhance and prolong the activity of TIDAL-01 by minimizing PD-1 driven T cell exhaustion in indications where anti-PD-(L)1 monotherapy has demonstrated little to no objective responses in clinical trials. Pembrolizumab will be dosed every three weeks until confirmed progressive disease or CR. The colorectal cancer patients and head and neck cancer patients under our investigator sponsored clinical trials in collaboration with Moffitt will also be receiving pembrolizumab as their anti-PD-(L)1 treatment on the same dosing schedule as described for our multi-site solid tumor trial. Notably, for all head and neck cancer patients across both trials, we will initiate manufacturing of TIDAL-01 from tumors extracted from patients newly diagnosed with metastatic disease who are anti-PD-(L)1 naïve. These patients will receive first line anti-PD-(L)1 treatment on trial and upon disease progression will immediately receive TIDAL-01 as their second line therapy.

Additionally as part of our multi-site solid tumor trial we are also exploring the inclusion of low dose radiation therapy, or LDRT as part of the conditioning regimen with the first dose of LDRT administered immediately prior to the TIDAL-01 infusion and the second dose administered following IL-2 treatment, prior to initiating pembrolizumab. Inclusion of LDRT as part of the conditioning regimen, has the potential to enhance T cell penetration into the tumor and reduce the inhibitory tumor stroma microenvironment to further potentiate the depth of response to TIDAL-01. Lastly, we are also exploring expansion into additional indications including non-small cell lung cancer.

The primary endpoint of both trials will be safety and tolerability of TIDAL-01, with secondary endpoints focusing on efficacy based on measures including ORR and durability of response. Additionally, TIDAL-01 clinical translational studies will include investigational endpoints, including TCR sequencing and detailed T cell subset immunophenotyping, that are designed to define the pharmacokinetic profile of the selected TIL drug products together with key aspects of pharmacodynamic profiles. These data will be correlated with clinical outcomes to enable future refinement of clinical dosing regimens and, in combination with drug product characterization data collected during manufacture, support the validation of mechanistically relevant potency release endpoints. We intend to provide an initial clinical update across these three trials in mid-2024.

TIDAL-02

Overview

TIDAL-02 is our next Selected TIL program where we are developing a next generation streamlined manufacturing process designed for selecting tumor-reactive T cells and additional modifications to enhance TIL quality and function. We believe that streamlined manufacturing has the potential to provide commercial advantages, as well as enable access to solid tumor indications where patients may progress rapidly. The TIDAL-02 manufacturing process targets less than three weeks of production time and will seek to employ a direct selection

process step that utilizes our proprietary combination of selection markers to select for the greatest breadth of tumor-reactive T cells without requiring sequencing or peptide generation. Additionally, we believe that enhancing quality, function, and phenotype of T cells has the potential to drive additional activity in solid tumors. To enhance Selected TIL quality and function, we are assessing two key strategies: (i) culture enhancements to improve and maintain quality and function of the Selected TILs during *ex vivo* cell expansion and (ii) evaluation of functional genetic modifications of the Selected TILs to ensure durable enhancements to TIL quality and persistence *in vivo*. We believe that TIDAL-02 has the potential to address the medical need in solid tumor indications that are distinct but complementary to TIDAL-01, with the goal of moving into earlier lines of therapy. TIDAL-02 is currently in preclinical development.

TIDAL-02 Process Parameters

We are currently assessing three key process parameters to guide development of our TIDAL-02 product candidate that will be advanced into IND enabling studies. These three process parameters include: direct selection, gene editing, and enhanced isolation and expansion, as described below.

- *Direct Selection*: Our direct selection process for TIDAL-02 will seek to utilize our proprietary combination of clinically defined selection markers to select for the greatest breadth of tumor-reactive T cells directly from the TIL population generated in the enhanced isolation process (see below). These selection markers are intended to be indication agonistic and have the potential to recognize cell surface receptors that are present only on the surface of tumor-reactive T cells. We will then physically sort the tumor-reactive T cells from the bystander cells that are not tumor-reactive, on the basis of these selection markers. Our ongoing collaboration with Dr. Simon Turcotte at CHUM is enabling us to screen and evaluate the application of our proprietary mix of direct selection markers across a broad range of solid tumors.
- *Gene Editing*: We are assessing and prioritizing clinically informed targets for functional genetic modifications that we believe may have the potential to drive durable TIL quality and persistence *in vivo*. These gene edits will be designed to modify the tumor-reactive T cells to proliferate while resisting exhaustion post infusion, minimize their dependance on exogenous IL-2 for *in vivo* proliferation, and maintain their potential to kill tumors in suppressive tumor microenvironments. We plan to introduce these genetic modifications into our sorted population of directly selected TILs.
- *Enhanced Isolation and Expansion*: We are developing a set of culture media supplements to enhance our isolation and/or expansion steps. These supplements incorporate a mix of cytokines with the potential to rejuvenate dysfunctional and/or exhausted T cells. We aim to use these enhancements to improve and maintain TIL quality and function in culture to deliver a high-quality infusion product.

Selected TIL and Viral Immunotherapy

Overview

We believe that we are strongly positioned to be a leader in leveraging viral immunotherapy to further increase the activity of our TIL therapies, if approved. Viruses are naturally adept at reprogramming the TME, and we believe that our proprietary viral immunotherapies can be tailored to drive the best combination approach for TILs.

We are initially evaluating viral immunotherapies in combination with our lead Selected TIL product candidate, TIDAL-01, via two approaches: (i) administration of virus prior to TIL extraction to optimize TIL harvest and broaden applicability to additional tumor types with low immune cell infiltration, and (ii) administration of virus following treatment with TIDAL-01 to optimize TIL trafficking and infiltration into solid tumors and to support the anti-tumor functions of infiltrating immune cells. We are currently evaluating the optimal viral immunotherapy for combination with TIDAL-01 to advance into clinical development.

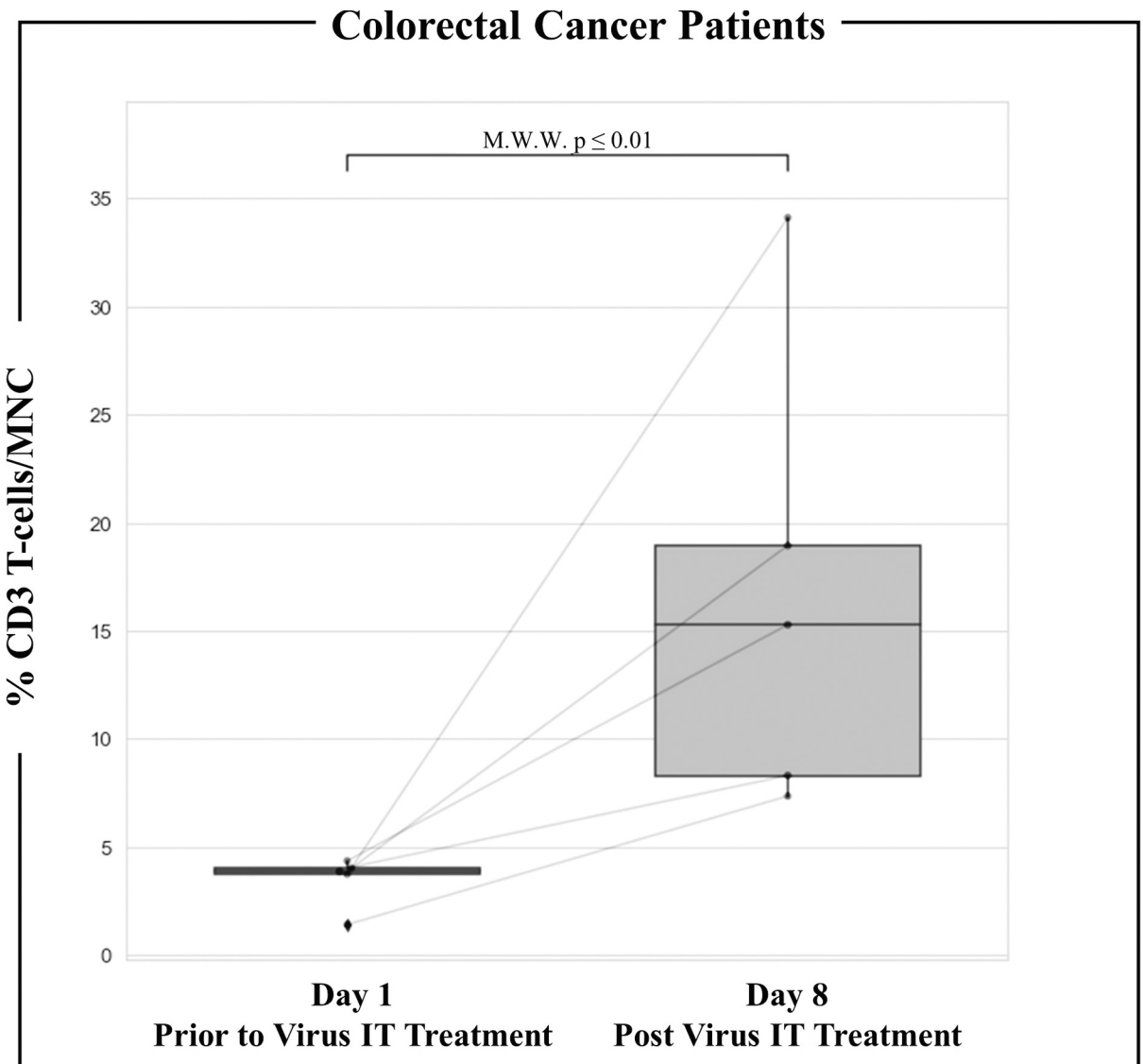
Selected TIL and Viral Immunotherapy Combination Strategies

- *TIDAL-01 + Virus Pre-treatment:* We believe that treating patients with virus, prior to surgical resection of the tumor sample, has the potential to drive a superior TIL harvest that can result in a more potent TIDAL-01 product for the patient. Intra-tumoral, or IT, administration of virus into the tumor site targeted for TIL resection has the potential to disrupt the tumor cells via oncolytic killing and expose new antigens to the immune system thus driving a larger and more diverse population of tumor-reactive T cells into the tumor bed. We believe that pre-treatment of a patient with virus will enable a superior TIL harvest, with the potential to increase the quality, quantity, and breadth of TILs. We plan to target this approach specifically to patients for whom and indications for which the TIL yield is typically low, often leading to failure in generating a therapeutic product for the patient.
- *TIDAL-01 + Virus Post-treatment:* Viral immunotherapy has the potential to reprogram the immunosuppressive tumor microenvironment (*e.g.,* turn a 'cold' tumor 'hot') potentiating TIL infiltration, function, and proliferation within the tumor. In addition, the presence of virus at the tumor site can serve as a beacon to call TILs to the site of the tumor. Treating the patient with virus following TIDAL-01 has the potential to increase the activity of TIDAL-01 treatment, if approved, across several challenging solid tumors. We believe this combination strategy has the potential for improved patient outcomes in indications with highly suppressive TMEs that typically are resistant to immune mediated treatment regimens.

Clinical Evidence Supporting Viral Immunotherapy Combination

In our clinical experience with viral immunotherapy, we have observed that viruses improved immune cell infiltration of the tumor and were well tolerated. Based on clinical experience with one of our proprietary viral immunotherapies, we have seen preliminary translational data supporting the biological rationale for combination of our Selected TILs with viral immunotherapies.

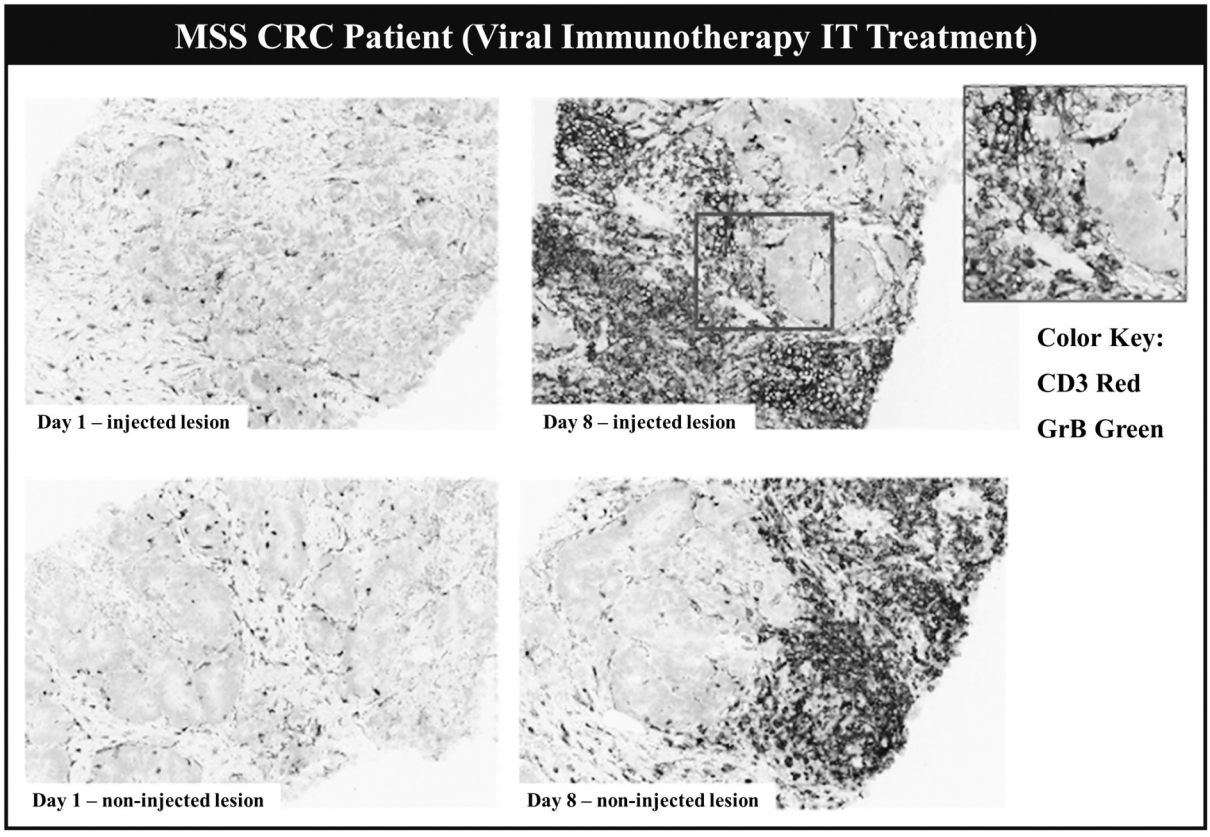
We conducted a clinical study with one of our proprietary viral immunotherapies between 2020 and 2022 where we enrolled and treated 18 patients in a dose escalation study for intra-tumoral delivery of our virus across multiple tumor types. Five of these 18 patients in the study had colorectal cancer and the graph below shows comparative translational data for all five colorectal cancer patients from this clinical trial. When comparing the paired tumor biopsies prior to and seven days following IT administration of our virus, we have observed increased T cell infiltration in the injected lesion across multiple colorectal cancer patients as evidenced in the graph below.



Box and whisker plot shows the median value (represented by the thick horizontal line), the first and third quartiles (represented by the bottom and top boxes, respectively) and the lower and upper vertical whiskers representing the maximum of 1.5x of the interquartile range

Serious adverse events in the trial included the following: two incidences of each of abdominal pain and pyrexia (meaning fever or an increase in body temperature above normal range), and one incident of each of sinus tachycardia (meaning an increase in heart rate with a normal rhythm while at rest), inappropriate antidiuretic hormone secretion (secretion of anti-diuretic hormone, a hormone that retains water in order to maintain appropriate water and salt balance via the kidney, outside of regular physiological release from the pituitary gland), ascites (meaning buildup of fluid in the abdomen), colitis (meaning inflammation of the colon), nausea, chills, systemic inflammatory response syndrome, cholecystitis (meaning inflammation of the gallbladder), enterocolitis infection (inflammation of small or large intestine as a result of infection by a pathogen), hyponatraemia (meaning abnormally low levels of sodium in the blood), dizziness, hypoaesthesia (meaning reduced sense of touch or sensation, or a partial loss of sensitivity to sensory stimuli), monoparesis (meaning partial loss of voluntary motor function in a single limb), acute respiratory failure, cough and haemorrhagic shock (meaning loss of blood or other fluid reducing the capacity of the heart unable to pump sufficient blood to the body). We have also observed that our proprietary

viruses turned “cold” tumors “hot” by driving T cells into tumors that were immunologically cold due to highly suppressive TMEs. This was exemplified by immunohistochemical evidence of increased CD3+ cells with a cytotoxic phenotype (granzyme B expression) in a MSS-colorectal cancer patient in both injected and non-injected tumors following IT administration of one of our proprietary viral immunotherapies.



We believe that these data suggest that our viral immunotherapies have the potential to increase the number of intra-tumoral T cells across multiple solid tumor types, including tumors with an immunosuppressive TME and provides support both pre- and post-treatment combination approaches with our Selected TIL pipeline programs.

Translational Assessment and Development Strategy

We are collaborating with the NCI to evaluate the generation of tumor-reactive T cells, which form the basis of our Selected TILs, from clinical tissue samples obtained from patients treated with our proprietary viral immunotherapies. NCI investigators are using NCI-developed methods and proprietary in vitro techniques to study lymphocytes derived from these patients, characterize their TCR specificity, and evaluate their persistence. We and the NCI plan to jointly analyze data and exchange information and expertise to advance the development of oncolytic viruses as a method for the generation of Selected TILs.

We are currently evaluating the optimal viral immunotherapy for combination with TIDAL-01 to advance into clinical development.

Manufacturing

We have established both internal and external technical operations, manufacturing, quality, and supply chain capabilities that support our pre-clinical and clinical assets. We have fully operational TIL cell therapy process and analytical development operations at our facility in San Diego, California. The site is approximately 20,000 square feet, and we have assembled an experienced team of cell therapy CMC experts. Our team of experts has completed

technology transfer of TIDAL-01 to our U.S.-based CDMO, Charles River Laboratories, and our manufacturing sciences group is fully enabled to support development efforts across our Selected TIL pipeline. As of December 31, 2023, our technical operations team is composed of 33 employees spanning expertise across core CMC functional areas, including upstream and downstream process development, bioanalytical sciences, formulation, process scale-up, technology transfer, quality control, manufacturing operations, packaging, distribution, and supply chain.

To support our TIDAL product candidate and pipeline programs, we have formed deep partnerships across a global network of CDMOs that specialize in bioprocess development, testing, cGMP manufacturing, formulation and filling, packaging, controlled temperature storage, and distribution. For TIDAL-01, this includes a close partnership with the Cell Therapy Facility at Moffitt Cancer Center, responsible for cGMP manufacturing, testing, release, and distribution of Selected TIL to the clinical investigators at Moffitt under our investigator sponsored clinical trials. We have separate partnerships, fully controlled and supervised by us, for the sequencing and peptide manufacturing portions of the TIDAL-01 manufacturing process. In parallel, we have completed a technology transfer of the TIDAL-01 Selected TIL manufacturing process to a U.S.-based CDMO. We intend for this to be our primary cGMP manufacturing partner for clinical supplies for TIDAL-01, to serve multiple clinical sites, independent and complimentary to our partnership with Moffitt. In addition to this core TIL cell therapy manufacturing network, we have a network of contract testing partners to fully enable our quality control and analytical release testing program, for our TIDAL pipeline that is managed by our internal quality control team. Except for the Moffitt sponsored TIDAL-01 clinical trial, all clinical trial materials for use in clinical trials are released, stored, and managed under our quality systems.

As clinical trial development progresses forward, technical operations will scale in a complimentary approach, exploring both internal capabilities as well as deepening and expanding external relationships to ensure we remain in full control of our CMC development, through commercialization.

Commercialization

We do not currently have a commercial organization for the marketing, sales, and distribution of products. We are advancing our clinical product candidate and pipeline programs for the treatment of patients with solid tumors, most of whom are treated in specialized treatment centers or hospitals.

We plan to build our global commercialization capabilities internally over time such that we are able to commercialize any product candidate for which we may obtain regulatory approval. While we hold global rights to our product candidates, we may selectively pursue strategic collaborations with third parties in order to maximize the commercial potential of our product candidates.

Competition

The biotechnology and pharmaceutical industries are characterized by the rapid evolution of technologies and understanding of disease etiology, significant investment, and a strong emphasis on intellectual property. While we believe that our differentiated scientific expertise in the field of cancer immunotherapy provides us with competitive advantages, we face potential competition from multiple sources, including major pharmaceutical, specialty pharmaceutical and existing or emerging biotechnology companies, as well as from academic institutions, governmental agencies, and public and private research institutions. We anticipate that we will face intense and increasing competition as new drugs and therapies enter the market and advanced technologies become available. Many of our competitors, either alone or with their strategic collaborators, have substantially greater financial, technical, and human resources than we do. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These entities also compete with us in recruiting and retaining qualified scientific, manufacturing, and management personnel and establishing clinical trial sites and patient enrollment in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may discover, develop, license, or commercialize products before or more successfully than we do.

We face competition from segments of the pharmaceutical, biotechnology, and other related markets that pursue the development of TIL or other cell therapies for the treatment of solid tumors. On February 16, 2024, FDA approved the first TIL therapy, Iovance Biotherapeutics Inc.’s lifileucel, for the treatment of unresectable or

metastatic melanoma. We are also aware of other companies that are developing TIL therapies include Achilles Therapeutics plc, Instil Bio, Inc., Intima Bioscience, Inc., KSQ Therapeutics, Inc., Lyell Immunopharma, Inc., Obsidian Therapeutics, Inc, and others. In addition, we may face competition from companies focused on CAR-T and TCR-T cell therapies for solid tumors, such as Adaptimmune Therapeutics PLC, Adicet Bio, Inc., Alaunos Therapeutics, Inc., Atara Biotherapeutics, Inc., and Immatics N.V. Other privately held biotechnology companies are evaluating neoantigen directed T cell approaches. We cannot predict whether new types of immunotherapies including novel checkpoint inhibitors may be enhanced and show greater efficacy, and we may have direct and substantial competition from such immunotherapies in the future. In addition, there are companies utilizing other cell-based approaches that may be competitive to our product candidates. More effective small molecules, cancer vaccines and other approaches may be developed and used as first line or second line treatments, which would reduce the opportunity for our Selected TIL therapies. Furthermore, we also face competition more broadly across the oncology market for cost-effective and reimbursable cancer treatments.

The most common methods of treating patients with cancer are surgery, radiation, and drug therapy, including chemotherapy, hormone therapy, biologic therapy, such as monoclonal and bispecific antibodies, immunotherapy, cell-based therapy and targeted therapy, or a combination of any such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our TIL product candidates, if any are approved, may compete with these existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our TIL products may not be competitive with them. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our TIL therapies that we successfully introduce to the market may pose challenges. In addition, many companies are developing new oncology therapeutics, and we cannot predict what the standard of care will be as our product candidates progress through clinical development. We could see a reduction or elimination in our commercial opportunity if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, are less expensive or with a more favorable label than our TIL product candidates. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Myst Merger Agreement

In December 2020, we entered into the Myst Merger Agreement, by and among our company, Flatiron Merger Sub I, Inc., or Merger Sub, Flatiron Merger Sub II, LLC, or Merger LLC, a direct, wholly-owned subsidiary of ours, Myst Therapeutics, Inc., or Myst, and Timothy Langer, the sole common stockholder of Myst, or Langer. Pursuant to the Myst Merger Agreement, the business combination, or the Merger, was effected in two steps. The first step was the merger of Merger Sub with and into Myst. The second step was the merger of Myst with and into Merger LLC. The Merger closed on December 14, 2020 and the effective date of the Merger was January 20, 2021. As a result of the Merger, the separate existences of Merger Sub and Myst ceased, and Merger LLC became our wholly-owned subsidiary.

Pursuant to the Myst Merger Agreement, on December 15, 2020, we paid the former equity holders of Myst, or the Myst Holders, a one-time up-front payment of $9.0 million in cash. We paid an additional cash consideration of $1.0 million to the Myst Holders on June 14, 2022. We also issued Langer 725,920 shares of our common stock. Of these shares, 362,960 shares of our common stock were issued upon the closing of the Merger and the remaining 362,960 shares were held in escrow with 25% vesting in December of each year that Langer remains our employee. As of December 31, 2023, Langer is still employed by our company and 272,220 shares of our common stock have vested and been released from escrow, with the remaining 90,740 shares of our common stock to be released over the next year based on his continued employment.

In addition, under the Myst Merger Agreement, each Myst Holder is entitled to receive certain payments as consideration based on the achievement by us of three predefined milestones. The initial milestone is the closing of an initial public offering, the second milestone is the first acceptance by the FDA of an IND filed by, on behalf of or for the benefit of us, or our sublicensees for a product being developed by or on behalf of us or our sublicensees that is claimed as a product or method of making or using the product by a pending or issued Myst patent claim existing

at the time of such acceptance, and the third milestone is the occurrence of the earlier of (i) the commencement of the first registration study for a product being developed by, on behalf of or for the benefit of us or our sublicensees that is claimed as a product or a method of making or using the product by an issued Myst patent claim existing as of the time of such commencement or (ii) the issuance of a Myst patent claim that claims a product or method of making or using the product then being developed by, on behalf of or for the benefit of us or our sublicensees, that is or was the subject of a registration study that has or had commenced. The milestones are not contingent on one another, and the milestones do not need to be achieved in any specific order.

Within 45 days of the achievement of the initial milestone, which occurred on July 25, 2023, we were obligated to pay the Myst Holders an aggregate amount equal to $3.0 million. At our election, we may pay this consideration in cash or in shares of our common stock. Pursuant to a letter agreement dated September 11, 2023 between us and the former equityholders of Myst regarding the $3.0 million milestone payment that became due and owing to the Myst Holders, we agreed to pay $0.2 million in cash to the former optionholders of Myst on or before September 30, 2023, with the remaining $2.8 million payable to Langer in shares of our common stock. On September 11, 2023, we issued 249,992 shares of our common stock to Langer.

Within 45 days of the achievement of the second milestone, we are obligated to pay the Myst Holders an aggregate amount equal to $10.0 million. At our election, we may pay this consideration in cash or in shares of our common stock. In May 2022, this milestone was achieved, and we elected to pay $5.0 million in shares of our common stock and $5.0 million in cash. We entered into a letter agreement dated July 25, 2022 with the former equityholders of Myst regarding the $10.0 million milestone payment that became due and owing to the Myst Holders, in which we agreed to pay to the former optionholders of Myst on or before July 28, 2022 $0.6 million in cash, with the remaining $9.4 million payable to Langer as follows: (i) on or before July 28, 2022, $2.2 million in cash, (ii) on or before July 31, 2022, $5.0 million in shares of our common stock and (iii) on or before January 10, 2023, $2.2 million in cash. On June 8, 2022, we issued Langer 212,203 shares of our common stock to settle the $5.0 million obligation payable in common stock. We then paid the Myst Holders $2.8 million in July 2022, with $2.2 million paid to Langer and $0.6 million paid to the remaining Myst Holders, and the remaining $2.2 million was paid to Langer in January 2023.

Within 45 days of the achievement of the third milestone, we are obligated to pay the Myst Holder an aggregate amount equal to $20.0 million. At our election, we may pay this consideration in cash or in shares of our common stock. If we elect to pay the Myst Holders this consideration in the form of shares of our common stock, then our existing stockholders will experience further dilution.

Pursuant to the Myst Merger Agreement, we had agreed to use commercially reasonable efforts to (i) cause a registration statement covering the sale on a continuous basis of the shares of our common stock to be declared effective as soon as reasonably practicable after filing such registration statement or (ii) register the resale of such shares of our common stock under an existing registration statement without amendment.

Collaboration Agreements

Moffitt Collaboration Agreements

Master Collaboration Agreement

In January 2021, we entered into an amended and restated master collaboration agreement, or the Moffitt Agreement, with Moffitt, to amend a then-existing master collaboration agreement from November 2019, as amended March 2020, between Moffitt and our now wholly-owned subsidiary, Myst Therapeutics LLC, with the intent to continue to work collaboratively in the research of cancer immunotherapies.

Each party granted the other party a right to use its research materials for performance of the research plans agreed to by the parties, or Research Plans. Each party granted the other party a non-exclusive, worldwide, sublicensable, perpetual, irrevocable, royalty-free license under all inventions invented in performance of a Research Plan and invented jointly by us and Moffitt, or Joint Inventions (with certain exclusions) to make, use, sell, offer for sale, import products and services and/or otherwise practice such inventions.

We granted Moffitt a royalty free, non-sublicensable, non-transferable, perpetual, non-exclusive license to use and practice certain inventions invented solely by us in the performance of a Research Plan for its internal non-commercial research purposes.

Moffitt granted us (i) a royalty-free, sublicensable, non-transferable, perpetual, non-exclusive license to use and practice certain inventions invented solely by Moffitt in the performance of a Research Plan, or Moffitt Inventions, (a) for internal, non-commercial research purposes outside the field of ACT and/or (b) to research, develop, make, use, sell, offer to sell, or import products and/or services in the field of ACT and (ii) a royalty free, sublicensable, non-transferable, perpetual, non-exclusive license to use and practice certain inventions invented in performance of a Research Plan or through the use of specified Moffitt research materials.

Moffitt granted us an option to obtain, with terms to be negotiated in good faith under commercially reasonable terms, a royalty-bearing, sublicensable exclusive license in the Moffitt Inventions, the TCR Inventions, and/or Moffitt's interest in Joint Inventions. We can exercise this option at any time within six months after Moffitt informs us of any new invention, and upon our exercise, the parties will have a period of six months to negotiate the terms of such exclusive license.

The Moffitt Agreement will expire upon the later of (i) four years from the effective date of the Moffitt Agreement or (ii) the termination or expiration of all Research Plans in effect under the Moffitt Agreement, unless extended upon mutual written agreement of the parties. Either party may terminate the Moffitt Agreement for cause upon any uncured breach by the other party or upon the insolvency of the other party.

Moffitt Alliance Agreement

In June 2022, we entered into a life science alliance agreement with Moffitt, or the Alliance Agreement, in order to further expand our relationship and support our existing agreements with Moffitt, or the Underlying Agreements. Pursuant to the Alliance Agreement, we will have priority access to Moffitt's scientific research, manufacturing, and clinical capabilities for the development of novel TIL therapies, including expedited clinical trial activation, enhanced patient screening and data sharing, access to Moffitt's cellular therapies research and development infrastructure, expanded molecular data sets and biospecimens for research, and allocated cGMP manufacturing capacity for our product candidates.

Under the Alliance Agreement, we are obligated to use commercially reasonable efforts to further develop TIL Products (as defined below), to manufacture TIL Products, to obtain regulatory approval for at least one TIL Product in the United States and to commercialize TIL Products in all countries in which regulatory approval for a TIL Product has been obtained. For purposes of the Alliance Agreement, TIL Product means any pharmaceutical, biopharmaceutical, or biotechnology TIL product that has been developed by us or Moffitt and is advanced into clinical development under an IND sponsored by Moffitt.

Pursuant to the Alliance Agreement, we have agreed to pay to Moffitt a total amount of at least $17.5 million, the Alliance Funding Amount, for research, development and manufacturing related services that will be paid in five equal annual installments on June 1st of each year starting on June 1, 2023. However, the aggregate amount we pay to Moffitt for all fees, costs, expenses and other payments pursuant to any Underlying Agreement with Moffitt entered into subsequent to February 7, 2022 may be credited against the Alliance Funding Amount. This reimbursement amount will be calculated annually at the conclusion of each payment period, and, to the extent our annual aggregate payments to Moffitt exceed the applicable annual installment amount, we will receive a reduction in the amount due for future installment payments based on a predetermined formula agreed to by the parties.

In connection with the execution of the Alliance Agreement, we issued Moffitt 91,721 shares of our common stock. As partial consideration under the Alliance Agreement, we also agreed to issue Moffitt an additional 366,884 shares of our common stock in the aggregate upon the satisfaction of certain clinical and regulatory milestones with respect to TIL Products. During the twelve months ended December 31, 2023, an additional 91,721 shares of common stock were issued to Moffitt as a result of the achievement of the milestone related to the start of the Phase 1 clinical trial for a TIL Product. In addition, upon achievement of certain thresholds for aggregate net sales of all TIL Products, we are required to make tiered sales-based milestones payments to Moffitt of up to an aggregate of $50.0 million. With respect to each of the equity and sales milestones described above, TIL Products include any

pharmaceutical, biopharmaceutical or biotechnology TIL product that is developed by us or Moffitt and is advanced into clinical development under an IND sponsored by Moffitt.

Unless earlier terminated, the Alliance Agreement will remain in effect for a term of five years and may be extended for additional periods upon the mutual written consent of both parties. Either party may terminate the Alliance Agreement in the event of (i) the other party's material breach of the Alliance Agreement that remains uncured after ninety days of receiving written notice of such breach (or in the case of breach of payment obligations, within ten days), (ii) the other party's insolvency and (iii) a pandemic event resulting in government lockdowns or orders that legally compel such party to cease operations or that result in material disruptions in the available workforce and prevents such party from performing its contractual obligations for a period of more than six months. At any time after June 1, 2025, either party may terminate the Alliance Agreement without cause upon sixty days prior written notice to the other party, or a Termination for Convenience. Upon a Termination for Convenience, the terminating party shall pay to the other party a termination fee in an amount equal to a low double digit percentage of the then remaining Alliance Funding Amount. Termination or expiry of one or more Underlying Agreements does not affect the term of the Alliance Agreement, which will continue to apply to the remaining ongoing Underlying Agreements.

Intellectual Property

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions, improvements and know-how related to our business; defend and enforce our patents and other intellectual property; preserve the confidentiality of our trade secrets; and operate without infringing or otherwise violating the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products and methods may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same. We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. See "Risk Factors—Risks Related to Our Intellectual Property."

We actively seek to protect our proprietary technology, inventions, and other intellectual property that is commercially important to the development of our business by a variety of means, such as seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also may rely on trade secrets and know-how relating to our proprietary technology platform, on continuing technological innovation and on in-licensing opportunities to develop, strengthen and maintain the strength of our position in the field of cell therapy that may be important for the development of our business. We may also seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets, as well as to manufacture and develop novel cell or viral therapy products. Additional regulatory protection may also be afforded through data exclusivity, market exclusivity and patent term extensions where available.

As of December 31, 2023, we own or exclusively license 11 issued U.S. patents and 78 issued foreign patents in Australia, Austria, Belgium, Brazil, Canada, China, France, Germany, Great Britain, Hong Kong, India, Ireland, Israel, Italy, Japan, Luxembourg, Mexico, Netherlands, and Spain. We currently own or exclusively license 17 pending U.S. patent applications, three U.S. provisional applications, two pending international PCT applications, and 74 pending foreign patent applications in Australia, Brazil, Canada, China, Europe, Hong Kong, Israel, Japan, Korea, Mexico, and New Zealand.

TIL Therapy, Including TIDAL-01

We own four patent families related to TIL therapy that are filed worldwide. The first TIL-001, includes 12 patent applications pending in Australia, Brazil, Canada, China, Europe, Hong Kong, India, Israel, Korea, Mexico, New Zealand and the United States. The TIL-001 patent applications are directed to a processing method for producing autologous T cells for the treatment of cancer and resulting cell therapy compositions, which, if issued,

are expected to expire in 2040, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

The second family, TIL-002, includes 13 patent applications pending in Australia, Brazil, Canada, China, Europe, Hong Kong, India, Israel, Japan, Korea, Mexico, New Zealand and the United States. The TIL-002 patent applications are related to further aspects of processes for producing a TIL therapy and related compositions and methods, and patents that issue from this family, if any, are expected to expire in 2040, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

The third family, TIL-003, includes 10 patent applications pending in Australia, Canada, China, Europe, Hong Kong, Israel, Japan, Korea, New Zealand and the United States. The TIL-003 patent applications are directed to methods of producing tumor-reactive T cell compositions using modulatory agents, and patents that issue from this family are expected to expire in 2040, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

The fourth family, TIL-004, includes 12 patent applications pending in Australia, Brazil, Canada, China, Europe, Israel, India, Japan, Korea, Mexico, New Zealand and the United States. The TIL-004 patent applications are directed to methods for ex vivo enrichment and expansion of tumor-reactive T cells and related compositions, and any patents that issue from this family are expected to expire in 2041, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

We additionally own an international PCT application directed to particular TIL compositions and related methods, in which, if patents from applications claiming priority to the application issue, the patents are expected to expire in 2044, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance renewal, annuity or other governmental fees.

We own three provisional application families, in which, if patents from applications claiming priority to these provisional applications issue, the patents are expected to expire in 2044, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees. One provisional application family is directed to particular TIL compositions and related methods, another provisional application family is directed to particular methods of dosing and combination therapies of TIL compositions, and a further provisional application family is directed to genetically modified TILs and methods of producing and using the same.

We have licensed two patent families covering particular vaccinia viruses from the University of Pittsburgh, including in combination with TILs and methods for producing TILs for adoptive cell therapy. One patent family includes one foreign granted patent in Australia, and patent applications are pending in Australia, Canada, China, Europe, Hong Kong, Japan, Korea, and the United States. The other patent family includes pending patent applications in the United States, China, Europe and Hong Kong. Any patents issuing from these families are expected to expire in 2038 and 2040, respectively, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

Orthopox/Vaccinia Viral Therapy

We own two patent families directed to oncolytic orthopox, e.g., vaccinia, modified viral compositions that may contain transgenes that encode therapeutic payloads, and methods of using and making such viral compositions.

One patent family, SKV-002, is co-owned with Ottawa Hospital Research Institute, and includes 10 patent applications pending in Australia, Canada, China, Europe, Hong Kong, Israel, Japan, Korea, Mexico, and the United States. The pending SKV-002 claims include claims directed to modified orthopoxvirus, e.g., vaccinia, compositions, including modified orthopoxvirus compositions that express particular transgenes, and methods for using the compositions for the treatment of various cancers. Patents that may issue from this family are expected to expire in 2039, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

The other patent family is an international PCT application, in which, if patents from applications claiming priority to the application issue, the patents are expected to expire in 2044, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance renewal, annuity or other governmental fees. The application family is directed to compositions of a recombinant vaccinia virus encoding a particular Natural Killer cell and T lymphocyte inhibitor.

Additional Miscellaneous Virus IP

The first family, TBI-001, is licensed and includes 28 granted patents, in particular, two granted patents in each of Austria, Belgium, Canada, China, France, Germany, Great Britain, Ireland, Italy, Japan, Luxembourg the Netherlands, Spain and the United States. One patent application is pending in the US. Granted TBI-001 patent claims include claims directed to particular recombinant rhabdovirus compositions and uses thereof for treatment of cancer. Patents that have issued or may issue from this family are expected to expire in 2027, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

The second family, TBI-002, is licensed and includes 12 granted patents, in particular, two United States patents and one granted patent in each of Austria, Belgium, China, France, Germany, Great Britain, Ireland, Luxemburg, the Netherlands and Spain. One patent application is pending in Canada. Granted TBI-002 patent claims include claims directed to methods of using particular recombinant rhabdovirus vectors that express a tumor antigen for treatment of cancer, and kits that comprise such vectors. Patents that have issued or may issue from this family are expected to expire in 2030, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

The third family, TBI-003, is licensed and includes 24 granted patents, in particular, two granted patents in each of Australia, Israel, Japan, Mexico and the United States and one granted patent in each of Austria, Belgium, Brazil, Canada, China, France, Germany, Great Britain, India, Ireland, Italy, Luxemburg, the Netherlands and Spain. Granted TBI-003 patent claims include claims directed to particular attenuated rhabdovirus compositions, and particular oncolytic rhabdovirus compositions, and uses thereof for killing hyperproliferative cells and treatment of cancer. Patents that issued from this family are expected to expire in 2030, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

The fourth family, TBI-004, is licensed and includes 5 granted patents, in particular, one granted patent in each of France, Germany, Great Britain, Japan and the United States. Granted TBI-004 patent claims include claims directed to methods of inducing an immunogenic response utilizing a viral particle encoding particular rhabdovirus proteins. Patents that issued from this family are expected to expire in 2032, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

The seventh family, TBI-007, is licensed and includes 5 granted patents, in particular, one granted patent in each of France, Germany, Great Britain, Hong Kong and the United States. Granted TBI-007 patent claims include claims directed to methods of inducing a contemporaneous synergistic oncolytic virus infection of a cancer cell utilizing particular pairs of oncolytic viruses wherein one virus expresses an interferon (IFN) binding protein and the second virus is unable to block IFN gene expression. Patents that issued from this family are expected to expire in 2029, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

The eighth family, TBI-009, is licensed and includes 5 granted patents, in particular, two granted United States patents and one granted patent in each of France, Germany and Great Britain. Granted TBI-009 patent claims include claims directed to compositions of an oncolytic virus encoding an FGF2 protein and a Type 1 interferon scavenger. Patents that issued from this family are expected to expire in 2034, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

The tenth family, TBI-017, is licensed. Patent applications are pending in Canada, China, Europe, Hong Kong, Japan and the United States. Pending TBI-017 patent claims include claims directed to vaccine compositions comprising peptide antigens and oncolytic virus adjuvants, and methods of using the compositions to induce an immune response. Patents that may issue from this family are expected to expire in 2039, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

We have licensed one patent family covering a method of treating cancer by combining adoptive cell therapy (ACT) and an oncolytic virus vaccine. The patent family includes eight granted patents, in particular, one granted patent in each of China, France, Germany, Great Britain, Hong Kong, Ireland, the Netherlands and the United States. The issued patent claims include claims directed to combination therapies, methods of treating cancer and methods of producing a population of cells. Patent applications are pending in Canada, China, Europe, Hong Kong and the United States. Any patents issuing from this family are expected to expire in 2037, without taking into account any possible patent term adjustment or extension and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

Government Regulation and Product Approval

Government authorities in the United States (at the federal, state and local level) and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, quality control, safety, effectiveness, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of biopharmaceutical products such as those we are developing.

Our product candidates must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory authority before they may be legally marketed in foreign countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in the European Union are addressed in a centralized way, but country-specific regulation remains essential in many respects. The process for obtaining regulatory approvals and the subsequent compliance with federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Product Development Process

In the United States, the FDA regulates biological products, or biologics, under the Federal Food, Drug and Cosmetic Act, or FDCA, the Public Health Service Act, or PHSA, and their implementing regulations. The process required by the FDA before a biological product may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests and animal studies according to good laboratory practices, requirements, or GLPs, and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- approval by an independent Institutional Review Board 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 GCPs and any additional requirements for the protection of human research patients and their health information, to establish the safety, purity and potency (or efficacy) of the proposed biological product for its intended use;
- submission to the FDA of a biologics license application, or BLA, seeking marketing approval that includes substantial evidence of safety, purity, and potency from results of nonclinical testing and clinical trials;

- 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 Advisory Committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with current good manufacturing practice requirements, or cGMPs, to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;
- potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA; and
- FDA review and approval of the BLA.

Before testing any biological product candidate, including our product candidates, in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical 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 preclinical tests must comply with federal regulations and requirements including GLPs. The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. 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 raises safety concerns or questions regarding the proposed clinical trials and places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA.

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 at the local level as set forth in the National Institutes of Health Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an Institutional Biosafety Committee, or 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, companies and other institutions not otherwise subject to the NIH Guidelines may voluntarily follow them.

Clinical trials involve the administration of the biological product candidate to patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an independent IRB at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial 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 study 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 studies and clinical study results to public registries.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The biological product is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety. These studies are designed to test the safety, dosage tolerance, absorption, metabolism, and distribution 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 biological product is evaluated in a limited patient population with a specified disease or condition to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for the specific targeted diseases or condition and to determine dosage tolerance, optimal dosage and dosing schedule. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk to benefit ratio of the product and provide an adequate basis for product approval.
- Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. During all phases of clinical development, regulatory authorities require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, and the investigators for serious and unexpected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar product, findings from, animal or in vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. In addition, during the development of a new biological product, sponsors are given opportunities to meet with the FDA at certain points, including prior to submission of an IND, at the end of Phase 2, and before a BLA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach alignment on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the product candidate.

Concurrently with clinical trials, companies usually complete additional studies and must also develop additional information about the physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements, and in the case of human cellular products such as TILs, good tissue practices or GTPs. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHSA emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

After the completion of clinical trials all required testing of a biological product in accordance with all applicable regulatory requirements, the results of product development, preclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product candidate for one or more indications. FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA submission must include results of all relevant data available from preclinical and clinical studies, 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 studies intended to test the safety and effectiveness of a use of the product candidate, or from a number of alternative sources, including studies initiated by independent investigators.

Under the Prescription Drug User Fee Act, as amended, or PDUFA, each BLA must be accompanied by a significant user fee. The FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual program fee for biological products. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency 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. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA's goal is to review standard applications within ten 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 the BLA to determine, among other things, whether the proposed product is safe, pure and potent for the proposed indication, and the facility in which it is manufactured, processed, packed or held meets standards designed to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. 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 generally inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements. To assure cGMP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. If the agency decides not to approve the BLA in its present form, the FDA will issue a complete response letter that describes all of the specific deficiencies in the BLA identified by the FDA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the complete response letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. For example,

the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product candidate and to enable patients to have continued access 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. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized, and may further limit marketing of the product based on the results of these post-marketing studies.

In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any product for an indication for which orphan designation has been granted. However, if only one indication for a product has orphan designation, a pediatric assessment may still be required for any applications to market that same product for the non-orphan indication(s).

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug or biologic for this type of disease or condition 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. The orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition 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 disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent 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. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

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, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Expedited Development and Review Programs

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new 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. As part of the fast track program, 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.

Any product, submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if the product candidate is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. The FDA will attempt to direct additional resources to the evaluation of an application for a new 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 ten months under standard review).

Additionally, a product may be eligible for accelerated approval. Products 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 approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other 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 addition, the FDA may grant breakthrough therapy designation to a product candidate for its indication under study. Breakthrough therapy designation is intended to expedite the development and review of products that are intended to treat serious or life-threatening conditions and that preliminary clinical evidence demonstrates that the product candidate, alone or in combination with other drugs and biologics, shows substantial improvement over currently available therapy on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If the FDA grants a breakthrough therapy designation, it may take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the product candidate to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and considering alternative clinical trial designs when scientifically appropriate, which may result in smaller trials or more efficient trials that require less time to complete and may minimize the number of patients exposed to a potentially less efficacious treatment. Breakthrough therapy designation comes with all of the benefits of fast track designation, which means that the sponsor may file sections of the BLA for review on a rolling basis if certain conditions are satisfied, including an agreement with FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same product if relevant criteria are met.

The FDA may also designate a product candidate as a regenerative medicine advanced therapy, or RMAT. The RMAT designation is intended to facilitate an efficient development program for, and expedited review of, any product candidate that meets the following criteria: (i) the product candidate 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 product candidate is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (iii) preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such a disease or condition. RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate, and eligibility for rolling review and priority review of BLAs. Cell therapy

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 sites, including through expansion to additional sites, as appropriate. RMAT-designated cell therapy candidates that receive accelerated approval may, as appropriate, fulfill their post-approval requirements through the completion of clinical studies, patient registries, or through submission of 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 the therapy.

Fast Track designation, priority review, accelerated approval, breakthrough therapy designation, 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.

Post-Approval Requirements

Biological products 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, providing the FDA with updated safety and efficacy information, product sampling and distribution, and advertising and promotion of the product.

In addition, quality control and manufacturing procedures must continue to conform to applicable manufacturing requirements after approval to ensure the long-term stability of the product. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMPs. Manufacturers and other entities involved in the manufacture and distribution of approved 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 cGMPs and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including, among other things, recall or withdrawal of the product from the market. In addition, changes to the manufacturing process are strictly regulated, and depending on the significance of the change, may require prior FDA approval before being implemented. Other types of changes to the approved product, such as adding new indications and claims, are also subject to further FDA review and approval.

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 label to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS. 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 studies;
- 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 that are in accordance with the provisions of the approved label. The FDA and other authorities 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. 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 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 a manufacturer's communications on the subject of off-label use of their products.

U.S. Marketing Exclusivity

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, amended the PHSA to authorize the FDA to approve similar versions of innovative biologics, commonly known as biosimilars. Biosimilarity, which requires that the biological product be highly similar to the reference product notwithstanding minor differences in clinically inactive components and 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 study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product 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.

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 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 preclinical 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.

Pediatric exclusivity is another type of regulatory 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 trial in accordance with an FDA-issued "Written Request" for such a trial.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our current and future operations are subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare & Medicaid Services, or CMS, other divisions of the U.S. Department of Health and Human Services, or HHS, (e.g., the Office of Inspector General, Office for Civil Rights and the Health Resources and Service Administration), the U.S. Department of Justice, or DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, our business practices, including our clinical research program and any future sales, marketing and scientific/educational grant programs may be required to comply with the anti-fraud and abuse

provisions of the Social Security Act, the false claims laws, transparency requirements, and similar state laws, each as amended, as applicable.

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, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Rather, if "one purpose" of the remuneration is to induce referrals, the federal Anti-Kickback Statute is violated. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on 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. 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. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor.

The civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to, among others, a federal healthcare program that the person knows or should know is for a medical or other item or service that was not provided as claimed or is false or fraudulent.

The federal false claims laws, including the federal False Claims Act, or FCA, impose significant penalties and can be enforced by private citizens through civil qui tam actions, prohibit, any person or entity from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal government, including federal healthcare programs such as Medicare and Medicaid, 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. For instance, historically, 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. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses. In addition, a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA.

The Health Insurance Portability and Accountability Act of 1996, or HIPAA created additional federal criminal statutes that prohibit, among other things, 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, willfully obstructing a criminal investigation of a healthcare offense, 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. Like the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, HIPAA, as amended by Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, imposes certain requirements on covered entities, which include certain healthcare providers, health plans and healthcare clearinghouses, and their business associates and covered subcontractors that receive or obtain protected health information in connection with providing a service on behalf of a covered entity relating to the privacy, security and transmission of individually identifiable health information.

Additionally, the federal Physician Payments Sunshine Act, or the Sunshine Act, 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) 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), certain non-physician practitioners (such as physician assistants and nurse practitioners), and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually to CMS certain ownership and investment interests held by physicians and their immediate family members. Failure to report accurately could result in penalties. In addition, many states also govern the reporting of payments or other transfers of value, many which differ from each other in significant ways, are often not pre-empted, and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts.

Also, many states have similar, and typically more prohibitive, 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. In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological 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 and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, 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 and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices.

Ensuring business arrangements with third parties comply with applicable healthcare laws and regulations is a costly endeavor. If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other current or future 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, individual 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, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non- compliance with these laws, 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, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations.

The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or also known as a formulary, which might not include all of the FDA-approved products for a particular indication. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be

considered medically necessary or cost-effective. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. In addition, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Further, obtaining reimbursement for our product may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of physicians. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

We may develop products that, once approved, may be administered by a physician. Under currently applicable U.S. law, certain products not usually self-administered (including injectable drugs) may be eligible for coverage under Medicare through Medicare Part B. Medicare Part B is part of original Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain biopharmaceutical products, that are medically necessary to treat a beneficiary's health condition. As a condition of receiving Medicare Part B reimbursement for a manufacturer's eligible drugs, the manufacturer is required to participate in other government healthcare programs, including the Medicaid Drug Rebate Program and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of HHS as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities that participate in the program.

Different pricing and reimbursement schemes exist in other countries. In the European Union, or EU, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other EU member states allow companies to fix their own prices for medicines, but monitor and control company profits. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. The downward pressure on the rise in healthcare costs in general and pharmaceutical products in particular has become intense. As a result, in the EU, increasingly high barriers are being erected to the entry of new products. In the United States, the emphasis on managed care, the increasing influence of health maintenance organizations, and additional legislative changes has increased and we expect will continue to increase the pressure on product pricing. In addition, coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell product candidates for which marketing approval is obtained. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, has substantially changed healthcare financing and delivery by

both governmental and private insurers. Among the ACA provisions of importance to the pharmaceutical and biotechnology industries, in addition to those otherwise described above, are the following: (i) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations; (ii) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs; (iii) expanded the availability of lower pricing under the 340B drug pricing program by adding new entities to the program; (iv) increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP; (v) expanded the eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, thereby potentially increasing manufacturers' Medicaid rebate liability; (vi) 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; and (vii) established a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been executive, legal and Congressional challenges to certain aspects of the ACA. 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. Further, prior to the U.S. Supreme Court ruling, President Biden issued an executive order that initiated 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 instructed certain governmental authorities 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. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.

On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or 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 and through a newly established manufacturer discount program. It is unclear how other healthcare reform measures, if any, will impact 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. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

Further legislation or regulation could be passed that could harm our business, results of operations and financial condition. Other legislative changes have been proposed and adopted since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included aggregate reductions to Medicare payments to providers, which went into effect beginning on April 1, 2013 and, due to subsequent legislative amendments, will stay in effect through 2032. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of 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.

More recently, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA

permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its product candidates available to eligible patients as a result of the Right to Try Act.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. 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 Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, 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 take effect progressively starting in fiscal year 2023. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. It is currently unclear how the IRA will be implemented but it is likely to have a significant effect on the pharmaceutical industry. Further, in response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical 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 expect additional state, federal and foreign healthcare reform measures to be adopted in the future, any of which could limit the amounts that federal, state and foreign governments will pay for health products, which could result in reduced demand for our products, if approved or additional pricing pressure.

For instance, in December 2021, the EU Regulation No 2021/2282 on Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once the Regulation becomes applicable, it will have a phased implementation depending on the concerned products. This regulation is intended to boost cooperation among EU member states in assessing health technologies, including new medicinal products, as well as certain high-risk medical devices, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or 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 the company 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.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Additional Regulation

In addition to the foregoing, state, federal and foreign laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Foreign Government Regulation

To market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products.

Whether or not we obtain FDA approval of 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. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions. The approval process varies from country to country, can involve additional testing beyond that required by FDA, and may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing, promotion, and reimbursement vary greatly from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Non-Clinical Studies and Clinical Trials

Similarly to the United States, the various phases of non-clinical and clinical research in the European Union, or EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice, as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

At the EU level, clinical trials are governed by the Clinical Trials Regulation (EU) No 536/2014, or CTR, which entered into application on January 31, 2022 repealing and replacing the former Clinical Trials Directive 2001/20, or CTD.

The CTR is intended to harmonize and streamline clinical trial authorizations, simplify adverse-event reporting procedures, improve the supervision of clinical trials and increase transparency. Specifically, the Regulation, which is directly applicable in all EU Member States, introduces a streamlined application procedure through a single-entry point, the "EU portal", the Clinical Trials Information System, or CTIS; a single set of documents to be prepared and submitted for the application; as well as simplified reporting procedures for clinical trial sponsors. A harmonized procedure for the assessment of applications for clinical trials has been introduced and is divided into two parts. Part I assessment is led by the competent authorities of a reference Member State selected by the trial sponsor and relates to clinical trial aspects that are considered to be scientifically harmonized across EU Member States. This assessment is then submitted to the competent authorities of all concerned Member States in which the trial is to be conducted for their review. Part II is assessed separately by the competent authorities and Ethics Committees in each concerned EU Member State. Individual EU Member States retain the power to authorize the conduct of clinical trials on their territory.

The extent to which on-going clinical trials will be governed by the CTR will depend on the duration of the individual clinical trial. For clinical trials in relation to which an application for approval was made on the basis of the CTD before January 31, 2023, the CTD will continue to apply on a transitional basis until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR. The CTR will apply to clinical trials from an earlier date if the related clinical trial application was made on the basis of the CTR or if the clinical trial has already transitioned to the CTR framework before January 31, 2025.

In all cases, clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Medicinal products used in clinical trials must be manufactured in accordance with Good Manufacturing Practice, or cGMP, and in a GMP licensed facility, which can be subject to GMP inspections. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorization

In order to market our future product candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization, or MA. To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a Marketing Authorization Application, or MAA, either under a centralized procedure administered by the European Medicines Agency, or EMA, or one of the procedures administered by the competent authorities of EU Member States (decentralized procedure, national procedure or mutual recognition procedure). An MA may be granted only to an applicant established in the EU.

The centralized procedure provides for the grant of a single MA by the European Commission that is valid throughout the EEA (which is comprised of the 27 EU Member States plus Norway, Iceland and Liechtenstein). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for (i) medicinal products derived from biotechnological processes, (ii) products designated as orphan medicinal products, (iii) advanced therapy medicinal products, or ATMPs, and (iv) products with a new active substance indicated for the treatment of HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, authorization through the centralized procedure is optional on related approval.

Under the centralized procedure, the EMA’s Committee for Medicinal Products for Human Use, or CHMP, conducts the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing MA. The maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP.

In exceptional cases, when a medicinal product targeting an unmet medical need is expected to be of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). The CHMP can, however, revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines, or PRIME, scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. The PRIME scheme is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Eligible products must target conditions for which there is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the EU or, if there is, the new medicinal product will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. Product developers that benefit from PRIME designation may be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and potentially accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development plan, future scientific advice, and regulatory strategies.

Unlike the centralized authorization procedure, the decentralized MA procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the Heads of Medicines Agencies' Coordination Group for Mutual Recognition and Decentralised Procedures – Human, or CMDh, for review. The subsequent decision of the European Commission is binding on all EU Member States.

The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU Member State to apply for this authorization to be recognized by the competent authorities in other EU Member States. Like the decentralized procedure, the mutual recognition procedure is based on the acceptance by the competent authorities of the EU Member States of the MA of a medicinal product by the competent authorities of other EU Member States. The holder of a national MA may submit an application to the competent authority of an EU Member State requesting that this authority recognize the MA delivered by the competent authority of another EU Member State.

An MA has, in principle, an initial validity of five years. The MA may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State in which the original MA was granted. To support the application, the MA holder must provide the EMA or the competent authority with a consolidated version of the Common Technical Document providing up-to-date data concerning the quality, safety and efficacy of the product, including all variations introduced since the MA was granted, at least nine months before the MA ceases to be valid. The European Commission or the competent authorities of the EU Member States may decide on justified grounds relating to pharmacovigilance, to proceed with one further five year renewal period for the MA. Once subsequently definitively renewed, the MA shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (for a centralized MA) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Moreover, in the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The European Commission may grant a conditional MA for a medicinal product if it is demonstrated that all of the following criteria are met: (i) the benefit-risk balance of the medicinal product is positive; (ii) it is likely that the applicant will be able to provide comprehensive data post-authorization; (iii) the medicinal product fulfils an unmet medical need; and (iv) the benefit of the immediate availability to patients of the medicinal product is greater than the risk inherent in the fact that additional data are still required. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are provided, it can be converted into a "standard" MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed.

Furthermore, MA may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. Similarly, to the conditional MA, an MA granted in exceptional circumstances is reserved to medicinal products to be authorized for treatment of rare diseases or unmet medical needs for which the applicant does not hold the complete data set legally required for the grant of a "standard" MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable.

Additional Requirements Applicable to Human Cells and Tissues-Based Products

Advanced Therapy Medicinal Products, or ATMPs, include gene therapy products as well as somatic cell therapy products and tissue engineered products. The grant of marketing authorization in the EU for products containing viable human tissues or cells such as gene therapy medicinal products is governed by Regulation (EC) No. 1394/2007 on ATMPs, read in combination with Directive (EC) No. 2001/83 of the European Parliament and of the Council, commonly known as the Community code on medicinal products. Regulation (EC) No. 1394/2007 establishes specific rules concerning the authorization, supervision and pharmacovigilance of gene therapy medicinal products, somatic cell therapy medicinal products and tissue engineered products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety and efficacy of their products to the EMA which is required to provide an opinion regarding the application for marketing authorization. The European Commission grants or refuses marketing authorization in light of the opinion delivered by the EMA.

Under EU law, cell-based products must also comply with Directive (EC) No. 2004/23 of the European Parliament and of the Council of March 31, 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells, or the Tissues and Cells Directive, as well as its technical implementing directives.

This Directive describes the conditions and quality requirements which must be applied when sourcing the cells intended for manufacturing of the cell-based medicinal product. EU directives not being of direct application, these requirements are implemented under national law, in each EU member state, and as such applicable requirements may vary from one EU member state to another, as each is free to implement measures which are more stringent than those set out under the Tissues and Cells Directive.

Amongst other things, the Tissues and Cells Directive requires the following:

- tissue and cell procurement and testing must be conducted by persons appropriately trained and experienced;
- tissue and cells establishments must in particular (i) be accredited, designated, authorized or licensed by the national competent authority, (ii) perform appropriate controls to ensure compliance with applicable requirements, (iii) maintain records of their activities, and (iv) implement a quality system based on good practices principles set out by the European Commission;

- a traceability system must be implemented such that the tissues and cells can be traced from the donor to the recipient, which includes appropriate labelling of said tissues and cells;
- import and export of human tissues and cells must be undertaken by establishments which are duly be accredited, designated, authorized or licensed by the national competent authority, and these tissues and cells must comply with the requirements set out under the Tissues and Cells Directive; and
- a system for the notification of serious adverse events and reactions must be implemented.

On December 14, 2022, a political agreement was reached on the European Commission's proposal for a regulation on standards of quality and safety for substances of human origin, intended for human application, or the SoHOs Proposal. Unlike directives, regulations are directly applicable, i.e., without the need for adoption of EU member state laws implementing them, in all EU member states. If adopted, the SoHOs Proposal would repeal, replace, and aggregate the existing regulatory framework applicable to human blood, tissue and cells, consisting of Directive 2002/98/EC on blood and blood components and the Tissue and Cells Directive. The SoHO proposal includes transitional provisions and, if formally adopted, the Regulation would apply 3 years after its adoption.

Data and Marketing Exclusivity

In the EU, innovative products granted an MA generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted data exclusivity prevents generic and biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the authorized innovative product (i.e., reference product), when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial MA of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical or biological entity, and products may not qualify for data exclusivity.

In the EU, there is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided in support of an application for MA, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

Orphan Medicinal Products

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. In the EU, Regulation (EC) No. 141/2000,as implemented by Regulation (EC) No. 847/2000 provides that a medicinal product can be designated as an orphan medicinal product if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life threatening or chronically debilitating condition (2) either (a) such condition affects not more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from the orphan status, would not generate sufficient return in the EU to justify the necessary investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized for marketing in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition.

Regulation (EC) No 847/2000 sets out further provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product. An application for the designation of a medicinal product as an

orphan medicinal product must be submitted at any stage of development of the medicinal product but before filing of an MAA. An MA for an orphan medicinal product may only include indications designated as orphan. For non-orphan indications treated with the same active pharmaceutical ingredient, a separate marketing authorization has to be sought. An EU orphan designation entitles a party to incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized procedure. Upon grant of a MA, orphan medicinal products are entitled to a ten years of market exclusivity for the approved indication, which means that the competent authorities cannot accept another MAA, or grant a MA, or accept an application to extend a MA for a similar medicinal product for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan, or PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The market exclusivity period 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 which it received orphan destination, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, MA may be granted to a similar product for the same indication at any time if (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant consents to a second orphan medicinal product application; or (iii) the applicant cannot supply enough orphan medicinal product.

Pediatric Development

In the EU, MAAs for new medicinal products have to include the results of studies conducted in the pediatric population, in compliance with a PIP agreed with the EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant clinical benefit over existing treatments for pediatric patients. Once the MA is obtained in all the EU member states and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted.

Post-Approval Requirements

Where an MA is granted in relation to a medicinal product in the EU, the holder of the MA is required to comply with a range of regulatory requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the EU member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, or QPPV, who is responsible for the establishment and maintenance of that system, and oversees the safety profiles of medicinal products and any emerging safety concerns. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAA must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to both EU and EU member states' laws governing the promotion of medicinal products, interactions with physicians, misleading and comparative

advertising and unfair commercial practices. General requirements for advertising and promotion of medicinal products, such as direct-to-consumer advertising of prescription medicinal products are established in EU law. However, the details are governed by regulations in individual EU Member States and can differ from one country to another. For example, applicable laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, which may require approval by the competent national authorities in connection with an MA. The SmPC is the document that provides information to physicians concerning the safe and effective use of the product. Promotional activity that does not comply with the SmPC is considered off-label and is prohibited in the EU.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Pricing, Coverage and Reimbursement

In the EU, pricing and reimbursement schemes vary widely from country to country. Some EU Member States may approve a specific price for a product, or they may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU Member States allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions.

In addition, some EU Member States may require the completion of additional studies that compare the cost-effectiveness of a particular medicinal product candidate to currently available therapies. This Health Technology Assessment, or HTA, process is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. In December 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA Regulation, was adopted. The HTA Regulation is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at EU level for joint clinical assessments in these areas. When it enters into application in 2025, the HTA Regulation will be intended to harmonize the clinical benefit assessment of HTA across the European Union. In light of the fact that the United Kingdom has left the EU, Regulation No 2021/2282 on HTA will not apply in the United Kingdom. However, the UK Medicines and Healthcare products Regulation Agency ("MHRA") is working with UK HTA bodies and other national organizations, such as the Scottish Medicines Consortium ("SMC"), the National Institute for Health and Care Excellence ("NICE"), and the All-Wales Medicines Strategy Group, to introduce new pathways supporting innovative approaches to the safe, timely and efficient development of medicinal products.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom's, or UK, withdrawal from the EU on January 31, 2020, commonly referred to as Brexit, has changed the regulatory relationship between the UK and the EU. The Medicines and Healthcare products Regulatory Agency, or MHRA, is now the UK's standalone regulator for medicinal products and medical devices. Great Britain (England, Scotland and Wales) is now a third country to the EU. Northern Ireland will, with regard to EU regulations, continue to follow the EU regulatory rules for now.

The UK regulatory framework in relation to clinical trials is governed by the Medicines for Human Use (Clinical Trials) Regulations 2004, as amended, which is derived from the CTD, as implemented into UK national law through secondary legislation. On January 17, 2022, the MHRA launched an eight-week consultation on reframing the UK legislation for clinical trials,and which aimed to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials.The UK Government published its response to the consultation on March 21, 2023 confirming that it would bring forward changes to the legislation. These resulting legislative amendments will determine how closely the UK regulations will align with the CTR. In October 2023, the MHRA announced a new

Notification Scheme for clinical trials which enables a more streamlined and risk-proportionate approach to initial clinical trial applications for Phase 4 and low-risk Phase 3 clinical trial applications.

Marketing authorizations in the UK are governed by the Human Medicines Regulations (SI 2012/1916), as amended. Since January 1, 2021, an applicant for the EU centralized procedure marketing authorization can no longer be established in the UK. As a result, since this date, companies established in the UK cannot use the EU centralized procedure and instead must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain a marketing authorization to market products in the UK. All existing EU marketing authorizations for centrally authorized products were automatically converted or grandfathered into UK marketing authorization, effective in Great Britain only, free of charge on January 1, 2021, unless the marketing authorization holder opted-out of this possibility. Northern Ireland currently remains within the scope of EU authorizations in relation to centrally authorized medicinal products. Accordingly, until the Windsor Framework is implemented in Northern Ireland on January 1, 2025, products falling within the scope of the EU centralized procedure can only be authorized through UK national authorization procedures in Great Britain.

The MHRA has also introduced changes to national marketing authorization procedures. This includes introduction of procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment route, a rolling review procedure and the International Recognition Procedure. Since January 1, 2024, the MHRA may rely on the International Recognition Procedure, or IRP, when reviewing certain types of marketing authorization applications. This procedure is available for applicants for marketing authorization who have already received an authorization for the same product from a reference regulator. These include the FDA, the EMA, and national competent authorities of individual EEA countries. A positive opinion from the EMA and CHMP, or a positive end of procedure outcome from the mutual recognition or decentralized procedures are considered to be authorizations for the purposes of the IRP.

There is no pre-marketing authorization orphan designation for medicinal products in the UK. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding marketing authorization application. The criteria are essentially the same as those in the EU, but have been tailored for the market. This includes the criterion that prevalence of the condition in Great Britain, rather than the EU, must not be more than five in 10,000. Upon the grant of a marketing authorization with orphan status, the medicinal product will benefit from up to 10 years of market exclusivity from similar products in the approved orphan indication. The start of this market exclusivity period will be set from the date of first approval of the product in Great Britain.

Rest of World Government Regulation

For other countries outside of Europe, such as some 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 must be 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 or our potential collaborators 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.

Employees and Human Capital Resources

As of December 31, 2023, we employed 80 employees, all of whom are full-time, consisting of clinical, research, operations, regulatory, and finance personnel. 25 of our employees hold Ph.D., M.D. or M.D. equivalent degrees. None of our employees is subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

We recognize that our continued ability to attract, retain and motivate exceptional employees is vital to ensuring our long-term competitive advantage. Our employees are critical to our long-term success and are essential to helping us meet our goals. Among other things, we support and incentivize our employees in the following ways:

- ***Talent development, compensation and retention***—We strive to provide our employees with a rewarding work environment, including the opportunity for growth, success and professional development. We provide a competitive compensation and benefits package, including broad-based bonus and equity plans, a 401(k) plan and a multi-layered recognition program—all designed to attract and retain a skilled and diverse workforce.
- ***Health and safety***—We support the health and safety of our employees by providing comprehensive insurance benefits, an employee assistance program, wellness days and other additional benefits which are intended to assist employees to manage their well-being.
- ***Inclusion and diversity***—We are committed to efforts to increase diversity and foster an inclusive work environment that supports our workforce.

Facilities

We have entered into a lease agreement for 19,474 square feet of space for our headquarters in San Diego, California, which expires in May 2025 with an option to extend up to another three years. We believe that our existing facility is adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms.

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. 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, such proceedings or claims 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 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 in this Annual Report on Form 10-K, including our 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 adversely affect our business, results of operations and financial condition. In any such 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 believe to be immaterial also may impair our business, results of operations and financial condition. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Annual Report on Form 10-K.

Risks Related to Our Business

We have limited operating history, have incurred substantial net losses and anticipate that we will continue to incur net losses for the foreseeable future. We have no products approved for commercial sale, have never generated any revenue from product sales and may never be profitable.

We are a clinical stage biotechnology company with a limited operating history. We were formed in 2014 and we have devoted substantially all of our efforts and financial resources to organizing and staffing our company, business planning, raising capital, discovering product candidates and securing related intellectual property rights, and conducting research and development activities for our Selected TIL programs and product candidates. Consequently, we have no meaningful operations upon which to evaluate our business and predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing program candidates. Investment in biotechnology product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. We have not yet demonstrated the ability to progress any product candidate through clinical trials, we have no products approved for commercial sale and we have not generated any revenue from product sales to date. We continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and we have incurred overall net losses since our inception through December 31, 2023. We had a net loss of $55.2 million and $30.8 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023 and December 31, 2022, we had an accumulated deficit of $176.8 million and $121.6 million, respectively. Additionally, we will not receive any additional collaboration revenue under the Takeda Agreement in the future because this agreement has been terminated. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of our Selected TIL programs, and seek regulatory approvals for our product candidates.

We anticipate that our expenses will increase substantially if, and as, we:

- advance the development of our lead Selected TIL product candidate TIDAL-01 through two Phase 1 clinical trials and, if the results are favorable, into further clinical development;
- actively advance our other preclinical pipeline programs, including TIDAL-02, our next Selected TIL program and our TIDAL-01 and viral immunotherapy combination program;
- seek regulatory approvals for any product candidates that successfully complete clinical trials, if any;
- increase the amount of research and development activities to identify and develop Selected TIL product candidates;
- hire additional clinical, quality control and scientific personnel;
- expand our operational, financial and management systems and increase personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- maintain, expand and protect our intellectual property portfolio;

- expand our external manufacturing relationships;
- oversee and maintain our manufacturing infrastructure;
- establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any products for which we may obtain marketing approval and intend to commercialize on our own or jointly with third parties; and
- invest in or in-license enabling technologies.

To become and remain profitable, we and any current or potential future collaborators must develop and eventually commercialize products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials, obtaining marketing approval for product candidates, manufacturing, marketing and selling products if we obtain marketing approval, obtaining market acceptance for such products and satisfying any post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and the price or of common stock, and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop and market additional product candidates. We also 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 revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' (deficit) equity and working capital.

We will require additional capital to fund our operations, and if we fail to obtain necessary capital on acceptable terms, or at all, we will not be able to complete the development and future commercialization of our current and any future product candidates.

Our operations have consumed substantial amounts of cash since our inception. We expect to continue to spend substantial amounts of cash to conduct further research and development, preclinical studies and clinical trials of our current and future product candidates, to seek regulatory approvals for our product candidates and to launch and commercialize any products if we receive regulatory approval.

We have three ongoing Phase 1 clinical trials for our lead Selected TIL product candidate, TIDAL-01, including a multi-site trial for the treatment of breast cancer, colorectal cancer, head and neck cancer and uveal melanoma, and and two investigator sponsored trials with Moffitt across colorectal cancer, head and neck cancer and both cutaneous and non-cutaneous melanomas. We intend to provide an initial clinical update across these two trials in mid-2024. We are also developing TIDAL-02, our next Selected TIL program, which is currently in preclinical development and we intend to evaluate the combination of TIDAL-01 with viral immunotherapy. We are currently evaluating the optimal viral immunotherapy for combination with TIDAL-01 to advance into clinical development.

As of December 31, 2023, we had approximately $94.8 million in cash, cash equivalents and short-term investments. Based on our current operating plan, we expect that our cash, cash equivalents and short-term investments will enable us to fund our operations for at least twelve months from the date of this Annual Report on Form 10-K. 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 in order to complete clinical development of any of our current programs. Our monthly spending levels will vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with development of our programs and product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and future commercialization activities, if any. Our future capital requirements will depend on many factors, including:

- the costs of conducting clinical trials;
- the progress of preclinical development for our programs and clinical trials of our current earlier-stage product candidates;
- the costs of manufacturing;
- the scope, progress, results and costs of discovery, preclinical development, laboratory testing and clinical trials for other potential product candidates we may develop, if any;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaborations and partnerships on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments to us or by us under any collaboration agreements we might have at such time;
- the costs of preparing, filing and prosecuting patent applications, obtaining, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our headcount growth and associated costs as we expand our business operations and research and development activities;
- the cost of operating as a public company;
- our ability to mitigate the impact of adverse macroeconomic conditions or geopolitical events, including the ongoing conflict between Ukraine and Russia, the ongoing conflict in the Middle East, recent bank failures or other factors on our preclinical and clinical development or operations;
- the costs and timing of future commercialization activities, if any, including product sales, marketing, manufacturing and distribution, if we receive marketing approval for any of our product candidates;
- our ability to achieve sufficient market acceptance, adequate coverage and reimbursement from third-party payors and adequate market share; and
- the amount of revenue, if any, received from commercial sales of our product candidates, if any of our product candidates receive marketing approval.

We do not have any committed external source of funds or other support for our development efforts and additional funding may not be available on acceptable terms, or at all. Market volatility resulting from adverse macroeconomic conditions or geopolitical events, including the ongoing conflict between Ukraine and Russia and in the Middle East, recent bank failures or other factors may further adversely impact our ability to access capital as and when needed. Until we can generate sufficient product or royalty revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other arrangements. If we raise additional funds through public or private equity offerings, the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Further, to the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, your ownership interest will be diluted. In addition, any debt financing may subject us to fixed payment obligations and covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. We also could be required to seek collaborators for our current or future product candidates at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may need to significantly delay, scale back or discontinue the development or future commercialization of one or more of our product candidates, if approved, or one or more of our other research and development initiatives and we may need to undertake additional workforce reductions or restructuring activities in the future. Any of the above events could

adversely affect our business, results of operations and financial condition and cause the price of our common stock to decline.

Our business is highly dependent on the success of our lead Selected TIL product candidate TIDAL-01, as well as our other current and any future product candidates. All of our product candidates will require significant additional preclinical or clinical development before we are able to seek regulatory approval for and launch a product commercially.

We are very early in our development efforts. If TIDAL-01 or any future product candidates encounter safety or efficacy problems, manufacturing failures, development delays or regulatory issues or other problems, our development plans and business may be significantly harmed.

We have three ongoing Phase 1 clinical trials for our lead Selected TIL product candidate, TIDAL-01, including a multi-site trial for the treatment of breast cancer, colorectal cancer, head and neck cancer, and and uveal melanoma, and two investigator sponsored trials with Moffitt across colorectal cancer, head and neck cancer and both cutaneous and non-cutaneous melanomas. We intend to provide an initial clinical update across these three trials in mid-2024. We are also developing TIDAL-02, our next Selected TIL program, which is currently in preclinical development and we intend to evaluate the combination of TIDAL-01 with viral immunotherapy. We are currently evaluating the optimal viral immunotherapy for combination with TIDAL-01 to advance into clinical development.

Our current and any future product candidates will require additional preclinical or clinical development, regulatory review and approval in one or more jurisdictions, substantial investment, and access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. We may not have the financial resources to continue development of, or to modify existing or enter into new collaborations for, any product candidate if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, our product candidates, including:

- negative or inconclusive results from our preclinical studies or clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- product-related side effects experienced by subjects in our clinical trials or by individuals using products or immunotherapies similar to our product candidates;
- delays in submitting INDs or comparable foreign applications or delays or failure in obtaining the necessary authorizations or approvals from regulators to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or comparable foreign regulatory authorities regarding the scope or design of our clinical trials;
- delays in enrolling subjects in clinical trials;
- high drop-out rates of subjects from clinical trials;
- inadequate supply or quality of product candidates or other materials necessary for the conduct of our clinical trials;
- greater than anticipated clinical trial costs;
- poor effectiveness of or safety issues associated with our product candidates during clinical trials;
- unfavorable FDA or comparable foreign regulatory authorities' inspection and review of a clinical trial site;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;

- potential disruptions caused by health pandemics or epidemics, including difficulties in initiating clinical sites, enrolling and retaining participants, diversion of healthcare resources away from clinical trials, travel or quarantine policies that may be implemented, and other factors;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular;
- varying interpretations of data by the FDA or comparable foreign regulatory authorities;
- manufacturing failures, including our TIL selection process, resulting in a less effective product candidate in the tumor indications we are pursuing; or
- unsuccessful improvements to our internal manufacturing processes.

The occurrence of any of the above events could adversely affect our business, results of operations and financial condition.

If we fail to develop and receive approval for our existing or any additional future product candidates, our commercial opportunity could be limited which could adversely affect our business, results of operations and financial condition.

Developing, obtaining marketing approval for, and commercializing any product candidates will require substantial additional funding and will be subject to the risks of failure inherent in medical product development. We may not be able to successfully advance any of our existing product candidates or any additional product candidates through the development process.

Even if we obtain approval from the FDA or comparable foreign regulatory authorities to market our existing or any additional product candidates for the treatment of solid tumors or any other indication, any such product candidates may not be successfully commercialized, widely accepted in the marketplace, or more effective than other commercially available alternatives. If we are unable to successfully develop and commercialize our existing or any additional product candidates, our commercial opportunity may be limited and our business, results of operations and financial condition may be adversely affected.

Unfavorable global economic conditions, including any adverse macroeconomic conditions or geopolitical events, including the conflict between Ukraine and Russia, the conflict in the Middle East, and recent bank failures affecting the financial services industry, could adversely affect our business, financial condition, results of operations or liquidity, either directly or through adverse impacts on certain of the third parties on which we rely to conduct certain aspects of our preclinical studies or clinical trials.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Global economic and business activities continue to face widespread uncertainties, and global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, rising inflation and monetary supply shifts, rising interest rates, labor shortages, declines in consumer confidence, declines in economic growth, increases in unemployment rates, recession risks, and uncertainty about economic and geopolitical stability. A severe or prolonged economic downturn, or additional global financial or political crises, could result in a variety of risks to our business, including delayed clinical trials or preclinical studies, delayed approval of our product candidates, delayed ability to obtain patents and other intellectual property protection, weakened demand for our product candidates, if approved, or our ability to raise additional capital when needed on acceptable terms, if at all. The extent of the impact of these conditions on our operational and financial performance, including our ability to execute our business strategies and initiatives in the expected timeframe, as well as that of third parties upon whom we rely, will depend on future developments which are uncertain and cannot be predicted. A weak or declining economy also could strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. Furthermore, our stock price may decline due in part to the volatility of the stock market and the general economic downturn.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation, or FDIC, as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership, and on May 1, 2023, First Republic Bank was also swept into receivership. Although a statement by the Department of the Treasury, the Federal Reserve and the FDIC indicated that all depositors of Silicon Valley Bank would have access to all of their money after only one business day of closure, including funds held in uninsured deposit accounts, borrowers under credit agreements, letters of credit and certain other financial instruments with Silicon Valley Bank, Signature Bank or any other financial institution that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder. If any of the banks which hold our cash deposits were to be placed into receivership, we may be unable to access such funds. As of December 31, 2023, all of our cash on deposit was maintained at two financial institutions in the United States, and our current deposits are in excess of federally insured limits. If further failures in financial institutions occur where we hold deposits, we could experience additional risk. Any such loss or limitation on our cash, cash equivalents and short-term investments would adversely affect our business. In addition, if any of the third parties on which we rely to conduct certain aspects of our preclinical studies or clinical trials are unable to access funds pursuant to such instruments or lending arrangements with such a financial institution, such parties' ability to fulfill their obligations to us could be adversely affected.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

We may evaluate various acquisitions and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness, contractual obligations or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party, their regulatory compliance status, and their existing products or product candidates and marketing approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business. Any of the foregoing may adversely affect our business, results of operations and financial condition.

We may not realize the expected benefits from our recent workforce reductions and it could result in total costs and expenses that are greater than expected and could disrupt our business.

In October 2022, we implemented a plan to consolidate our operations, which included moving our headquarters to San Diego, California and a reduction in our workforce. In addition, in June 2023, we conducted an additional reduction in our workforce. The changes to our operations and the reductions in workforce may yield unintended consequences and costs, such as the loss of institutional knowledge and expertise, attrition beyond our intended reductions in force, and a reduction in morale among our remaining employees, all of which may have an adverse effect on our development activities, our business, results of operations or financial condition. If we are unable to realize the expected operational efficiencies, our business, results of operations and financial condition would be adversely affected. In addition, to the extent we do not realize such anticipated operational efficiencies, we may need to undertake additional workforce reductions or restructuring activities in the future. Furthermore, our reductions in force may be disruptive to our operations. For example, our workforce reductions could yield unanticipated consequences, such as attrition beyond planned staff reductions, increased difficulties in our day-to-day operations and reduced employee morale. If employees who were not affected by the reductions in force seek alternative employment, this could result in our seeking contractor support at unplanned additional expense or harm our productivity. Our workforce reductions could also harm our ability to attract and retain qualified management, scientific, clinical, and manufacturing personnel who are critical to our business. Any failure to attract or retain qualified personnel could prevent us from successfully developing our potential product candidates. We may also discover that the reductions in workforce could make it difficult for us to pursue new opportunities and initiatives and require us to hire qualified replacement personnel, which may require us to incur additional and unanticipated costs and expenses. Our failure to successfully accomplish any of the above activities and goals may have a material adverse impact on our business, results of operations and financial condition.

Our ability to use our net operating loss carryforwards to offset future income could be subject to limitation.

As of December 31, 2023, we had approximately $43.0 million of U.S. federal and $81.9 million of state net operating loss, or NOL, carryforwards. Our U.S. federal NOL carryforwards can be carried forward indefinitely, but use of such carryforwards is limited to 80% of taxable income. If not utilized, our state NOL carryforwards will begin to expire at various dates beginning in 2038. These NOL carryforwards could expire unused and be unavailable to offset future income tax liabilities if we are not able to generate sufficient taxable income to utilize our state NOL carryforwards before they expire. We have recorded a full valuation allowance related to our carryforwards due to the uncertainty of the ultimate realization of the future benefits of those assets.

Furthermore, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, the amount of benefits from our NOL carryforwards may be impaired or limited if we incur a cumulative ownership change of more than 50% over a three-year period. Any future offerings of our securities may trigger such an ownership change. In addition, because we will need to raise substantial additional funding to finance our operations, we may in the future undergo further ownership changes. We have not conducted an analysis as to whether such a change of ownership has occurred, but if such a change has occurred or occurs in the future, we will be limited regarding the amount of NOL carryforwards that can be utilized annually in the future to offset taxable income. Any such annual limitation may significantly reduce the value of our NOL carryforwards before they expire, which could result in greater tax liabilities than we would incur in the absence of such a limitation.

We may have exposure to greater-than-anticipated tax liabilities, which could seriously harm our business.

The tax laws applicable to our international business activities, including the laws of the United States and other jurisdictions, are subject to change and uncertain interpretation. The U.S. government may enact significant changes to the taxation of business entities including, among others, the imposition of additional minimum taxes and an increase in the corporate tax rate. Any such change could have a significant impact on our cash flow.

Our income tax obligations are based on our corporate operating structure and third-party and intercompany arrangements, including the manner in which we develop, value, and use our intellectual property and the valuations of our intercompany transactions. The taxing authorities of the jurisdictions in which we operate may challenge our methodologies for valuing developed technology, intercompany arrangements, or transfer pricing, which could increase our worldwide effective tax rate and the amount of taxes we pay and seriously harm our business. Taxing

authorities also may determine that the manner in which we operate our business is not consistent with how we report our income, which could increase our effective tax rate and the amount of taxes we pay and seriously harm our business. In addition, our future income taxes could fluctuate because of earnings being lower than anticipated in jurisdictions that have lower statutory tax rates and higher than anticipated in jurisdictions that have higher statutory tax rates, by changes in the valuation of our deferred tax assets and liabilities. We are subject to regular review and audit by U.S. federal and state and foreign tax authorities. Any adverse outcome from a review or audit could seriously harm our business. In addition, determining our worldwide provision for income taxes and other tax liabilities requires significant judgment by management, and there are many transactions where the ultimate tax determination is uncertain. Although we believe that our estimates are reasonable, the ultimate tax outcome may differ from the amounts recorded in our financial statements for such period or periods and may seriously harm our business.

Exchange rate fluctuations may adversely affect our business, results of operations and financial condition.

We have operations, including employing a portion of our workforce, in Ottawa, Canada. Owing to the international scope of our operations, fluctuations in exchange rates between the U.S. dollar and the Canadian dollar may adversely affect our business, results of operations and financial condition. As a result, our business and the price of our common stock may be affected by fluctuations in foreign exchange rates, which may have a significant impact on our results of operations and cash flows from period to period. Currently, we do not have any exchange rate hedging arrangements in place.

Risks Related to Our Operations

We will need to grow the size of our organization, and we may experience difficulties in managing this growth, which could adversely affect our business.

As of December 31, 2023, we had 80 full-time employees. As our clinical development and future commercialization plans and strategies develop, and as we transition into operating as a public company, we may need to hire additional managerial, clinical, regulatory, sales, marketing, financial, legal and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our development efforts effectively, including the clinical and FDA or comparable foreign regulatory authorities review process for our current product candidates and any future product candidates, while complying with our contractual obligations to contractors and other third parties;
- developing and managing our internal manufacturing operations effectively and in a cost-effective manner while increasing production capabilities for our product candidates to commercial levels;
- identifying and establishing additional facilities for our operations; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize our product candidates, if approved, will depend, in part, on our ability to effectively manage any future growth. Our management may have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including contract manufacturers and companies focused on antibody development and discovery activities. The services of independent organizations, advisors and consultants may not continue to be available to us on a timely or cost-efficient basis when needed, and we may not be able to find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality, accuracy or quantity of the services provided is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain, or may be substantially delayed in obtaining, regulatory approval of our product candidates or otherwise advance our business.

We may not be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees, consultants and contractors as necessary, we may not be able to successfully implement the tasks necessary to further develop and commercialize our current or any future product candidates, if approved, and, accordingly, may not achieve our research, development and future commercialization goals, which could adversely affect our business.

If we lose key management or other scientific or medical personnel, or if we fail to recruit additional highly skilled personnel, our business, results of operations and financial condition could be adversely affected.

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 executive officers and other members of our management team, including our President and Chief Executive Officer, Sammy Farah, M.B.A., Ph.D. We do not currently maintain "key person" life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals. The loss of the services of any of our executive officers or other members of our management team, including our scientific and medical personnel, and our inability to find suitable replacements in a timely manner could result in delays in product development and adversely affect our business, results of operations and financial condition.

We conduct our operations at our facility in San Diego, California. This region is headquarters to many other biopharmaceutical and biotechnology companies and many academic and research institutions. Competition for skilled personnel in our industry is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options that vest over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are 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. Generally, employment agreements with our key employees provide for at-will employment, which means that such employee could leave our employment at any time, with or without notice. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior scientific and medical personnel.

Our internal information technology systems, or those of our third-party contract research organizations, contract manufacturing organizations and other contractors and consultants, may fail or suffer security breaches, loss or leakage of data and other disruptions, which could result in a material disruption of our development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability, and could adversely affect our business, results of operations and financial condition.

We are increasingly dependent upon information technology systems to operate our business. In the ordinary course of business, we collect, store and transmit confidential information (including, but not limited to, intellectual property, confidential and proprietary business information and personal information). It is critical that we do so in a secure manner to maintain the confidentiality and integrity of all such information. We also have outsourced elements of our operations to third parties, and as a result we manage a significant number of third-party contractors who have access to our confidential information.

Despite the implementation of security measures, given the size and complexity and the increasing amounts of confidential information that our information technology systems maintain, such systems and those of our third-party contract research organizations, or CROs, and contract manufacturing organizations and other contractors and consultants are potentially vulnerable to attack, breakdown, damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business

partners and/or other third parties, or from cyberattacks by malicious third parties (including the deployment of harmful malware, ransomware, malicious code, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our information technology system infrastructure or lead to data leakage. We may face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and reputational damage and the further development and future commercialization of our current product candidates or any future product candidates could be delayed.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach, our data protection efforts and our investment in information technology may not in the future prevent significant cyber incidents in our systems and those of our third-party contract research organizations and contract manufacturing organizations and other contractors and consultants that could adversely affect our business, results of operations and 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 any of 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 or security breaches in our internal information technology systems and those of our third-party contract research organizations and contract manufacturing organizations and other contractors and consultants 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 adversely affect our business, results of operations and financial condition. Further, we do not currently maintain cybersecurity liability insurance coverage.

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could adversely affect our business, results of operations and financial condition.

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to (1) comply with the laws of the FDA or comparable foreign regulatory authorities, (2) provide true, complete and accurate information to the FDA or comparable foreign regulatory authorities, (3) comply with manufacturing standards we have established, (4) comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws, or (5) report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA or comparable foreign regulatory authorities' approval of any of our product candidates and begin commercializing those products in the United States or abroad, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. It is not always possible to identify and deter misconduct by our employees, independent contractors, consultants, commercial partners and vendors. The precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from

governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in any of the following: the imposition of civil, criminal and administrative penalties, damages, monetary fines, individual imprisonment, disgorgement, possible exclusion from participation in government healthcare programs, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings and the curtailment of our operations.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit future commercialization of our product candidates, if approved, which could adversely affect our business, results of operations and financial condition.

We face an inherent risk of product liability as a result of testing our product candidates, including our current and any of our future product candidates in clinical trials and will face an even greater risk if we commercialize any products, if approved. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. Any such product liability claims could include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims also could be asserted under state consumer protection acts. Product liability claims could delay or prevent completion of our development programs. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit future commercialization of our product candidates, if approved. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- inability to bring a product candidate to the market, if approved;
- decreased demand for our products;
- injury to our reputation;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by U.S. and foreign regulators;
- costs to defend the related litigation;
- diversion of management's time and our resources;
- substantial monetary awards or settlements to trial participants;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate, if approved; and
- decline in our stock price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the future commercialization, if approved, of products we develop alone or with collaborators. We need to obtain additional insurance for clinical trials as our current pre-clinical and any future pre-clinical programs enter the clinical development phase. However, we may be unable to obtain, or may obtain on unfavorable terms, clinical trial insurance in amounts adequate to cover any liabilities from any of our clinical trials. Our insurance policies also may have various deductibles and exclusions, and we may be subject to a product liability claim for which we have no coverage. We may need to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, enforcing such indemnification provisions may

cause diversion of management's time and our resources and such indemnification may not be available or adequate should any claim arise.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could adversely affect our business, results of operations and financial condition.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our research and development activities involve the use of biological and hazardous materials and produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials, which could cause an interruption of our future commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, this may not be the case and we may not eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes or our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. Although we have environmental liability insurance for our San Diego facility as required by the related lease agreement, we do not currently carry specific biological waste or hazardous waste insurance coverage, workers compensation or property and casualty and general liability insurance policies that include coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

Our insurance policies may be inadequate and potentially expose us to unrecoverable risks.

We have limited director and officer insurance and commercial insurance policies. Any significant insurance claims would have a material adverse effect on our business, results of operations and financial condition. Insurance availability, coverage terms and pricing continue to vary with market conditions. We endeavor to obtain appropriate insurance coverage for insurable risks that we identify; however, we may fail to correctly anticipate or quantify insurable risks, we may not be able to obtain appropriate insurance coverage, and insurers may not respond as we intend to cover insurable events that may occur. We have observed rapidly changing conditions in the insurance markets relating to nearly all areas of traditional corporate insurance. Such conditions have resulted in higher premium costs, higher policy deductibles and lower coverage limits. For some risks, we may not have or maintain insurance coverage because of cost or availability.

Our operations are concentrated in one location, and we or the third parties upon whom we depend may be adversely affected by earthquakes, pandemics or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our current operations are predominantly located in San Diego, California. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, health epidemic, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our third-party contract manufacturers, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. Earthquakes, pandemics or other

natural disasters could further disrupt our operations and have a material and adverse effect on our business, results of operations and financial condition. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, the amounts of insurance may not be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third-party contract manufacturers, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed and our clinical trials may be delayed. Any business interruption may adversely affect our business, results of operations and financial condition.

Risks Related to Research and Development

The successful development of biopharmaceuticals is highly uncertain.

The successful development of biotechnology is highly uncertain and is dependent on numerous factors, many of which are beyond our control. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons including:

- preclinical study results may show the product candidate to be less effective than desired or to have harmful or problematic side effects;
- clinical trial results may show the product candidates to be less effective than expected (*e.g.,* a clinical trial could fail to meet its primary endpoint(s)), to have unacceptable side effects or toxicities or to have effects in humans that differ from previously observed effects in lab animals;
- failure to receive the necessary regulatory approvals or a delay in receiving such approvals. Among other things, such delays may be caused by slow enrollment in clinical trials, patients withdrawing from clinical trials, length of time to achieve trial endpoints, additional time requirements for data analysis, or BLA, or comparable foreign application, preparation, discussions with the FDA or comparable foreign regulatory authorities and any such request for additional preclinical or clinical data, or unexpected safety or manufacturing issues or failures;
- manufacturing costs, formulation issues, pricing or reimbursement issues, or other factors that make a product candidate uneconomical; and
- the proprietary rights of others and their competing products and technologies that may prevent or otherwise make it uneconomical for one or more of our product candidates from being commercialized, if approved.

The length of time necessary to complete clinical trials and to apply for marketing approval for a final decision by a regulatory authority varies significantly from one product candidate to the next and may be difficult to predict. Even if we are successful in getting market approval, commercial success of any approved products also will depend in large part on the availability of coverage and adequate reimbursement from third-party payors, including government payors such as the Medicare and Medicaid programs, commercial insurers, and managed care organizations, which may be affected by existing and future healthcare reform measures designed to reduce the cost of healthcare. Third-party payors could require us to conduct additional studies, including post-marketing studies related to the cost effectiveness of a product, to qualify for reimbursement, which could be costly and divert our resources. If third-party payors were to decide to not provide coverage and adequate reimbursement levels for any of our products, if approved, market acceptance and commercial success would be reduced.

In addition, if any of our product candidates are approved for marketing, we will be subject to significant regulatory obligations regarding the submission of safety and other post-marketing information and reports and registration, and will need to continue to comply (or ensure that our third-party providers comply) with cGMPs or

similar foreign requirements and good clinical practices, or GCPs, for any clinical trials that we conduct post-approval. GCPs are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. In addition, there always is the risk that we or a regulatory authority might identify previously unknown problems with a product post-approval, such as adverse events of unanticipated severity or frequency. Compliance with these requirements is costly, and any failure to comply or other issues with our product candidates following approval, if any, could adversely affect our business, results of operations and financial condition.

Clinical development involves a lengthy and expensive process, with uncertain outcomes. We may incur significant costs and/or experience delays in completing, or ultimately be unable to complete, the development of our current and future product candidates, including our lead product candidates.

To obtain the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe, pure and potent or effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain.

Differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data often are susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products.

Successful completion of clinical trials is a prerequisite to submitting a BLA, to the FDA, a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, and similar marketing applications to comparable foreign regulatory authorities, for each product candidate and, consequently, the ultimate approval and commercial marketing of any product candidates. We do not know whether any of our clinical trials will be completed on schedule, if at all.

We may experience delays in initiating or completing clinical trials. We also may experience numerous unforeseen events during, or as a result of, any future clinical trials that we could conduct that could delay or prevent our ability to receive marketing approval or commercialize our current product candidates or any future product candidates, including:

- regulators or institutional review boards, or IRBs, may not authorize, or ethics committees may not issue favorable opinions permitting us or our investigators to commence or continue a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of any product candidates may fail to show safety, purity or potency, or produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- we may experience manufacturing failures, including in our TIL selection process, resulting in a less effective product candidate in the tumor indications we are pursuing;
- the number of subjects required for clinical trials of any product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or subjects may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;

- we may elect to, or regulators, or IRBs or ethics committees may require that we or our investigators, suspend, vary, or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of any product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate to initiate or complete a given clinical trial; for example, the process development for TILs is very complicated and requires significant logistics, and any issues with this process could delay our trials;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, or IRBs or ethics committees to suspend or terminate the trials, or reports from clinical testing of other therapies may raise safety or efficacy concerns about our product candidates; and
- the FDA or comparable foreign regulatory authorities may require us to submit additional data such as long-term toxicology studies, or impose other requirements before permitting us to initiate a clinical trial.

We also could encounter delays if a clinical trial is suspended or terminated by us, the IRBs or ethics committees of the institutions in which such trials are being conducted, or the FDA or comparable foreign regulatory authorities, or recommended for suspension or termination by the Data Safety Monitoring Board, or DSMB, or foreign equivalent for such trial. A suspension or termination may be imposed by the FDA or comparable foreign 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 resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials also may ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA or comparable foreign regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials.

Our product development costs will increase if we experience delays in clinical testing or marketing approvals. We do not know whether any of our clinical trials will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations. Any delays in our clinical development programs may adversely affect our business, results of operations and financial condition.

In addition, the FDA's and comparable foreign regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the European Union, or EU, evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each EU Member State, leading to a single decision for each EU Member State. The assessment procedure for the authorization of clinical trials has been harmonized as well, including a joint assessment by all EU Member States concerned, and a separate assessment by each EU Member State with respect to specific requirements related to its own territory, including ethics rules. Each EU Member State's decision is communicated to the sponsor via the centralized EU portal. Once the clinical trial approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies.For clinical trials in relation to which application for approval was made on the basis of the Clinical Trials Directive before January 31, 2023, the Clinical Trials Directive will continue to apply on a transitional basis until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR. The CTR will apply to clinical trials from an earlier date if the related clinical trial application was made on the basis of the CTR

or if the clinical trial has already transitioned to the CTR framework before January 31, 2025. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

In light of the entry into application of the CTR on January 31, 2022, we may be required to transition clinical trials for which we have obtained regulatory approvals in accordance with the CTD to the regulatory framework of the CTR. Transition of clinical trials governed by the CTD to the CTR will be required for clinical trials which will have at least one site active in the E.U. on January 30, 2025. A transitioning application would need to be submitted to the competent authorities of E.U. Member States through the Clinical Trials Information Systems and related regulatory approval obtained to continue the clinical trial past January 30, 2025. This would require financial, technical and human resources. If we are unable to transition our clinical trials in time, the conduct of those clinical trials may be negatively impacted.

The regulatory framework in the United Kingdom, or UK, in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation). On January 17, 2022, the UK Medicines and Healthcare products Regulatory Agency, or MHRA, launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022. The reframe aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. On March 21, 2023, the MHRA published the outcome of the consultation with its responses confirming that it would bring forward changes to the legislation. These resulting legislative amendments will determine how closely the UK regulations will align with the CTR. Failure of the UK to closely align its regulations with the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and/or make it harder to seek a marketing authorization for the Company's product candidates on the basis of clinical trials conducted in the United Kingdom.

Preclinical development is uncertain. Our preclinical programs may experience delays or generate unfavorable data, and may never advance to clinical trials, which would adversely affect our ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all, and any of these events would adversely affect our business, results of operations and financial condition.

Before we can commence clinical trials for any product candidate in our preclinical programs, we must complete extensive preclinical studies that support our planned INDs in the United States, or similar applications in other jurisdictions. Our preclinical studies may not be completed on a timely basis and have an unfavorable outcome, and the FDA and comparable foreign regulatory authorities may not accept our proposed clinical programs, or the outcome of our preclinical studies may not ultimately support the further development of our preclinical programs. As a result, we may not be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and submission of INDs or similar applications may not result in the FDA or comparable foreign regulatory authorities allowing clinical trials to begin.

Our product candidates are based on a novel approach to the treatment of cancer, which makes it difficult to predict the time and cost of product candidate development.

We have concentrated substantially all of our recent research and development efforts on product candidates based on our Selected TIL approach, and our future success depends largely on the successful development of these approaches. Any development problems we experience in the future may cause significant delays or unanticipated costs, and such development problems may not be solved. Should we encounter development problems, including unfavorable preclinical or clinical trial results, the FDA and comparable foreign regulatory authorities may refuse to authorize us to conduct additional clinical trials, and even if they do, they may not approve our product candidates, or may require additional information, tests, or trials, which could significantly delay product development and significantly increase our research and development costs. Moreover, even if we are able to provide to the FDA or comparable foreign regulatory authorities the requested information or trials, the FDA or comparable foreign regulatory authorities may not accept them and may not approve our product candidates. We also may experience delays in developing a sustainable, reproducible and scalable manufacturing process, or developing or qualifying and validating product release assays, other testing and manufacturing methods, and our equipment and facilities in a timely manner. This may prevent us from completing our clinical trials or commercializing our product candidates on a timely or profitable basis, if at all.

In addition, the clinical trial requirements of the FDA and comparable foreign regulatory authorities and the criteria these regulators use to evaluate the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The FDA and comparable foreign regulatory authorities have limited experience with the approval of Selected TIL immunotherapies.

The manufacture of our product candidates is complex, and we may encounter difficulties in production, particularly with respect to process development, quality control, or scaling-up of any future manufacturing capabilities. If we, or any of our third-party manufacturers encounter such difficulties, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

Our product candidates are biologics and the process of manufacturing our product candidates is complex, highly regulated and subject to multiple risks. The manufacture of our product candidates involves complex processes, including harvesting tumor fragments from patients, isolating the T-cells from the tumor fragments, multiplying the T-cells to obtain the desired dose, and ultimately infusing the T-cells back into a patient. As a result of the complexities, the cost to manufacture biologics is generally higher than traditional small molecule chemical compounds, and the manufacturing process is less reliable and is more difficult to reproduce. Further, as a result of the complexities, we may not be able to successfully manufacture Selected TILs, which could result in any of our product candidates not being differentiated from a bulk TIL product, and as a result, any of our product candidates may not be effective in the tumor indications that we are pursuing. Moreover, our manufacturing process is susceptible to product loss or failure due to logistical issues associated with the collection of tumor fragments, or starting material, from the patient, shipping such material to the manufacturing site, shipping the final product back to the patient, and infusing the patient with the product, manufacturing issues associated with the differences in patient starting material, interruptions in the manufacturing process, contamination, equipment failure, assay failures, improper installation or operation of equipment, vendor or operator error, inconsistency in cell growth, meeting pre-specified release criteria, and variability in product characteristics. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. If for any reason we lose a patient's starting material, or later developed product at any point in the process, or if any product does not meet the applicable specifications, the manufacturing process for that patient will need to be restarted, including resection of the proper amount of tumor fragment and the resulting delay may adversely affect that patient's outcome. If microbial, viral, environmental or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.

Because our product candidates are manufactured specifically for each individual patient, we will be required to maintain a chain of identity with respect to the patient's tumor as it moves from the patient to the manufacturing facility, through the manufacturing process, and back to the patient. Maintaining such a chain of identity is difficult and complex, and failure to do so could result in adverse patient outcomes, loss of product, or regulatory action including withdrawal of our products from the market. Further, as product candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials or otherwise necessitate the conduct of additional studies.

As a result of these challenges, we may experience delays in our clinical development and/or commercialization plans, if approved. Furthermore, we may ultimately be unable to reduce the cost of goods for our product candidates to levels that will allow for an attractive return on investment if and when those product candidates are commercialized.

The manufacture of cell therapy products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of cell therapy products often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel, and compliance with strictly enforced federal, state, local and foreign regulations.

Externally, to support both TIDAL-01 and TIDAL-02, we have formed deep partnerships across a global network of contract development and manufacturing organizations, or CDMOs, that specialize in bioprocess development, testing, cGMP manufacturing, formulation and filling, packaging, controlled temperature storage, and distribution. For TIDAL-01, this includes a close partnership with the Cell Therapy Facility at Moffitt Cancer Center, responsible for cGMP manufacturing, testing, release, and distribution of Selected TIL to the clinical investigators at Moffitt under our investigator sponsored clinical trial. We have separate partnerships, fully controlled and supervised by us, for the sequencing and peptide manufacturing portions of the TIDAL-01 manufacturing process. In parallel, we have completed a technology transfer of the TIDAL-01 Selected TIL manufacturing process to a U.S.-based CDMO, Charles River Laboratories. Any problems or delays we, Moffitt or our CDMOs experience in preparing for commercial scale manufacturing of a product candidate or component may result in a delay in the FDA or comparable foreign regulatory authority approval of the product candidate or may impair our ability to manufacture commercial quantities or such quantities at an acceptable cost, which could result in the delay, prevention, or impairment of clinical development and commercialization of our product candidates, if approved, and could adversely affect our business.

Moreover, we may not succeed in maintaining our relationships with our current CDMOs or establishing relationships with additional or alternative CDMOs. Our product candidates may compete with other products and product candidates for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that are both capable of manufacturing for us and willing to do so. If our CDMOs should cease manufacturing for us, we would experience delays in obtaining sufficient quantities of our product candidates for clinical trials and, if approved, commercial supply. Further, our CDMOs may breach, terminate, or not renew its agreements with us. If we were to need to find alternative manufacturing facilities it would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. The commercial terms of any new arrangement could be less favorable than our existing arrangements and the expenses relating to the transfer of necessary technology and processes could be significant.

We are ultimately responsible for the manufacture of our product candidates. A failure to comply with these requirements may result in regulatory enforcement actions against our manufacturers or us, including fines and civil and criminal penalties, which could result in imprisonment, suspension or restrictions of production, injunctions, delay or denial of product approval or supplements to approved products, clinical holds or termination of clinical trials, warning or untitled letters, regulatory authority communications warning the public about safety issues with the biologic, refusal to permit the import or export of the products, product seizure, detention, or recall, operating restrictions, suits under the civil False Claims Act, corporate integrity agreements, consent decrees, or withdrawal of product approval.

Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, results of operations and financial condition.

Cell-based therapies and biologics rely on the availability of reagents, specialized equipment, and other specialty materials, which may not be available to us on acceptable terms or at all. For some of these reagents, equipment, and materials, we rely or may rely on sole source vendors or a limited number of vendors, which could impair our ability to manufacture and supply our products.

Manufacturing our product candidates requires many reagents, which are substances used in our manufacturing processes to bring about chemical or biological reactions, and other specialty materials and equipment, some of which are manufactured or supplied by small companies with limited resources and experience to support commercial biologics production. We currently depend on a limited number of vendors for certain materials and equipment used in the manufacture of our product candidates. Some of these suppliers may not have the capacity to support clinical trials and commercial products manufactured under cGMPs by biopharmaceutical firms or may otherwise be ill-equipped to support our needs. We also do not have supply contracts with many of these suppliers and may not be able to obtain supply contracts with them on acceptable terms or at all. Accordingly, we may experience delays in receiving key materials and equipment to support clinical or commercial manufacturing.

For some of these reagents, equipment, and materials, we rely and may in the future rely on sole source vendors or a limited number of vendors. 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.

Changes in product candidate manufacturing, formulation or analytical methods may result in additional costs or delay, which could adversely affect our business, results of operations and financial condition.

As product candidates are developed through preclinical studies to later-stage clinical trials towards approval and future commercialization, it is common that various aspects of the development program, such as manufacturing methods, formulation or analytical methods, are altered throughout the development process in an effort to optimize processes and results. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials or utilizing different analytical methods. Such changes also may require additional testing, or notification to, or authorization by the FDA or a comparable foreign regulatory authority. This could delay completion of clinical trials, require the conduct of bridging clinical trials or studies, require the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and/or jeopardize our ability to commence product sales and generate revenue.

Use of our product candidates could be associated with side effects, adverse events or other properties or safety risks, which could cause us to suspend or discontinue clinical trials, abandon a product candidate, delay or preclude approval, prevent market acceptance, limit the commercial profile of an approved label or result in other significant negative consequences that could severely harm our business, results of operations and financial condition.

Before obtaining regulatory approvals for the commercial sale of any of our products, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our current product candidates, including our lead product candidates, and any future product candidate are both safe, pure and potent, or effective for use in such product candidate's target indication. Clinical testing is expensive, can take many years to complete and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to generate desired safety and efficacy data despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence clinical trials are never approved and there can be no assurance that any of our clinical trials will ultimately be successful or support further clinical development of our current product candidates or any of our future product candidates or ultimately their approval.

Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. 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 comparable foreign regulatory authorities. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, results of operations and financial condition significantly.

If our product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the trial, or result in potential product

liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may harm our business, results of operations and financial condition significantly.

Patients in our ongoing and planned clinical trials may in the future suffer significant adverse events or other side effects not observed in our preclinical studies or previous clinical trials. In addition, if our product candidates are used in combination with other therapies, our product candidates may exacerbate adverse events associated with the therapy. Patients treated with our product candidates may also be undergoing surgical, radiation or chemotherapy treatments, which can cause side effects or adverse events that are unrelated to our product candidate, but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses.

If significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA, other comparable foreign regulatory authorities or an IRB or ethics committee may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially harm our business, results of operations and financial condition.

Additionally, if any of our product candidates receives regulatory approval, and we or others later identify undesirable side effects caused by such product, a number of potentially significant negative consequences could result. For example, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits of treatment with such product candidate outweigh the risks for each potential patient, which may include, among other things, a communication plan to health care practitioners, patient education, extensive patient monitoring or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry. Other potentially significant negative consequences include that:

- we may be forced to suspend marketing of that product, or decide to remove the product from the marketplace, if approved;
- regulatory authorities may withdraw or change their approvals of that product;
- regulatory authorities may require additional warnings on the label or limit access of that product to selective specialized centers with additional safety reporting and with requirements that patients be geographically close to these centers for all or part of their treatment;
- we may be required to create a medication guide outlining the risks of the product for patients, or to conduct post-marketing studies;
- we may be required to change the way the product is administered;
- we could be subject to fines, injunctions, or the imposition of criminal or civil penalties, or be sued and held liable for harm caused to subjects or patients; and
- the product may become less competitive, and our reputation may suffer.

Any of these events could diminish the usage or otherwise limit the commercial success of our product candidates and prevent us from achieving or maintaining market acceptance of the affected product candidate, if approved by applicable regulatory authorities.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected, which could adversely affect our business, results of operations and financial condition.

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. The enrollment of patients depends on many factors, including:

- the patient eligibility and exclusion criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will withdraw from the trials before completion.

In addition, our clinical trials will compete with other clinical trials for patient participation for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because 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. For example, we will compete with various other cancer therapies, including combinations studies. Public perception of TIL-based immunotherapies also may adversely influence willingness of subjects to participate in clinical trials. Furthermore, because the number of qualified clinical investigators 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 sites.

Further, if we implement improvements to our manufacturing process, we may decide to slow or limit enrollment while we are implementing such improvements. While we would expect such implementation to only be temporary, any resulting enrollment delays may adversely affect our business, results of operations and financial condition.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our future clinical trials, which could prevent completion of these trials and adversely affect our business, results of operations and financial condition.

Interim, "top-line," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available 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 preliminary or topline data from our 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. As a result, the topline or preliminary 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 and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the topline or preliminary data we previously published. As a result, topline and preliminary data should be viewed with caution until the final data are available.

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

Further, others, including regulatory authorities, 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 or product, and our company in general. In addition, the information we choose to publicly disclose regarding a particular clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. 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 our product candidates may be harmed, which could harm our business, results of operations or financial condition.

Due to our limited resources and access to capital, we must prioritize development of certain programs and product candidates; these decisions may prove to be wrong and may adversely affect our business, results of operations and financial condition.

Because we have limited financial and human resources, we intend to initially focus on research programs and product candidates for a limited set of indications. For example, we are initially focused on the development of our lead Selected TIL product candidate TIDAL-01 in breast cancer, colorectal cancer, uveal melanoma and both cutaneous and non-cutaneous melanomas. Because TIL therapy is a relatively new and expanding area of novel therapeutic interventions, there are many uncertainties related to development, marketing, reimbursement and the commercial potential for our product candidates. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We may for a number of reasons fail to identify viable new product candidates for clinical development from our current or future research programs. If we fail to identify additional potential product candidates, our business, results of operations and financial condition could be adversely affected.

Research programs to pursue the development of our existing and planned product candidates for additional indications and to identify new product candidates and disease targets require substantial technical, financial and human resources whether they are ultimately successful or not. Our research programs may initially show promise in identifying potential indications and/or product candidates, yet fail for a number of reasons to yield results for clinical development, including:

- the research methodology used may not be successful in identifying potential indications and/or product candidates;
- potential product candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective products against the indicated disease; or
- it may take greater human and financial resources than we will possess to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, thereby limiting our ability to develop, diversify and expand our product portfolio.

Accordingly, we may never be able to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential product candidates or other potential programs that ultimately prove to be unsuccessful.

We may seek orphan drug designation for our product candidates, but we may be unable to obtain such designation or to obtain or maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our product revenue, if any, to be reduced.

Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a biologic as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population of 200,000 or more in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States.

In the United States, orphan drug designation entitles a party to financial incentives such as tax advantages and user fee waivers. Opportunities for grant funding toward clinical trial costs may also be available for clinical trials of drugs or biologics for rare diseases, regardless of whether the biologics are designated for the orphan use. In addition, if a biologic with an orphan drug designation subsequently receives the first marketing approval for the disease or condition for which it has such designation, the product is entitled to a seven-year period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug for the same disease or condition for that time period, except in limited circumstances. If our competitors are able to obtain orphan drug exclusivity prior to us, for products that constitute the "same drug" and treat the same diseases or conditions as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

In the EU, the European Commission, following a related opinion of the EMA Committee for Orphan Medicinal Products, may grant orphan drug designation for medicinal products to be developed (i) for the diagnosis, prevention or treatment of diseases that are life-threatening or chronically debilitating, for which (ii) either (a) such conditions affect not more than 5 in 10,000 persons in the EU when the application is made, or (b) the product without the benefits derived from orphan status, would not generate sufficient return in the EU to justify the necessary investment in developing the medicinal product; and (iii) there exists no satisfactory authorized method of diagnosis, prevention, or treatment of the condition that has been authorized in the EU, or even if such method exists, the product will be of significant benefit to those affected by that condition.

If a drug with orphan designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug may be entitled to a period of marketing exclusivity. This precludes the FDA or the EMA from accepting another marketing application for the same drug or, in the case of the EMA, accept an application to extend for a similar product and the European Commission cannot grant a marketing authorization, for the same indication during this time period. The applicable period is seven years in the United States and ten years in the EU. The period which may be extended by six months in the United States and two years in the EU for products that have complied with the respective regulatory authority's agreed upon pediatric investigation plan. The exclusivity period in the EU can be reduced to six years if at the end of the fifth year a drug no longer meets the criteria for orphan drug designation, including where it can be demonstrated on the basis of available evidence that the drug is sufficiently profitable that market exclusivity is no longer justified or where the prevalence of the condition has increased above the threshold.

We may seek orphan designation for certain of our product candidates. However, we may be unsuccessful in obtaining orphan drug designation for these and may be unable to maintain the benefits associated with orphan drug designation, even if we do obtain such designation. Even if we obtain orphan drug designation and obtain orphan drug exclusivity for any of our product candidates, that exclusivity may not effectively protect those product candidates from competition because different products can be approved for the same disease or condition. Even after an orphan drug is granted orphan exclusivity and approved, the FDA can subsequently approve a later application for the same drug for the same disease or condition before the expiration of the seven-year exclusivity period if the FDA concludes that the later drug is clinically superior in that it is shown to be safer in a substantial portion of the target populations, more effective or makes a major contribution to patient care. Similarly, the European Commission can approve a similar drug for the same therapeutic indication during the 10-year-exclusivity if the original applicant consents thereto, if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities of the drug in the EU, or if the similar product is demonstrated to be safer, more effective or otherwise clinically superior to ours. In addition, 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. Moreover, 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 if we are unable to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the

development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We may attempt to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated approval pathways. If we are unable to obtain such approval, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA or comparable foreign regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA or comparable foreign regulatory authorities may seek to withdraw accelerated approval.

We may in the future seek an accelerated approval for our one or more of our product candidates. However, because our product candidates are in early development, there can be no assurance that the FDA would approve any form of application for expedited review for any of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful clinical benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. If such post-approval studies fail to confirm the product's clinical benefit, the FDA may withdraw its approval. Furthermore, the FDA's accelerated approval pathways do not guarantee an accelerated review by the FDA, and even if our product candidates could be granted a designation or qualify for expedited development, it would not increase the likelihood that such product candidate will receive FDA approval.

In the EU, under the centralized procedure, the EMA's Committee for Medicinal Products for Human Use may perform an accelerated assessment of a marketing authorization application. Applicants requesting an accelerated assessment procedure must justify that the product candidate targeting an unmet medical need is expected to be of major public health interest, particularly from the point of view of therapeutic innovation.

Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA or similar foreign regulatory authorities and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit a BLA or similar application for accelerated approval or any other form of expedited development or review. Similarly, there can be no assurance that after subsequent FDA or similar foreign regulatory authorities' feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development or review, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or other expedited development or review for our product candidates, there can be no assurance that such submission or application will be accepted or that any expedited development or review will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development or review for our product candidate would result in a longer time period to commercialization of such product candidate, if any, could increase the cost of development of such product candidate, and could harm our competitive position in the marketplace.

The FDA and other regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If any of our product candidates are approved and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. The FDA and other foreign regulatory authorities strictly regulate the promotional claims that may be made about prescription products, such as our product candidates, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other foreign regulatory authorities 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 U.S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The government has also required companies to enter into consent decrees or imposed permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Risks Related to the Biotechnology Industry

We face significant competition and if we fail to compete effectively, our business, results of operations and financial condition could be adversely affected.

The biotechnology and pharmaceutical industries are characterized by intense competition, fierce defense of intellectual property and rapidly advancing technologies. Our competitors may be able to develop other therapies or drugs that are able to achieve similar or better results than our product candidates. Our competitors include major pharmaceutical, specialty pharmaceutical and existing or emerging biotechnology companies, academic institutions, governmental agencies, and public and private research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well-established sales forces, and other biopharmaceutical companies may compete by establishing collaborative arrangements with these large companies. Smaller or early-stage companies also may prove to be significant competitors, particularly as they develop novel approaches to treating disease indications that our product candidates also are focused on treating. Established biotechnology companies may also invest heavily to accelerate discovery and development of novel therapeutics or to in-license novel therapeutics that could make the product candidates that we develop obsolete. Mergers and acquisitions in the biotechnology industry may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety, tolerability, reliability, durability, convenience of use, price and reimbursement.

We anticipate competing with other companies that are focused on treating disease indications that our product candidates also are focused on treating. A competitor may develop technologies focused on the same disease pathway as our technology or may focus on treating the targeted disease in a completely different manner. Our competitors may also seek and obtain patent rights to their technologies that are similar to ours, and such patent rights may in the future affect the direction of our product development or require us to negotiate a license to such patent rights. To the extent a new drug is developed by a competitor that is more efficacious than any product candidate developed by us, this could reduce or negate the need for our product candidate. In addition, while we believe our product candidates may be used in conjunction with existing or emerging standard of care in certain disease indications, as companies continue to improve upon existing standards of care, more efficacious drug therapies could become available, reducing or completely negating the benefit of our product candidates. Our competitors also may include companies that are or will be developing therapies for the same therapeutic areas that we are targeting within our early pipeline.

We face competition from segments of the pharmaceutical, biotechnology and other related markets that pursue the development of TIL or other cell therapies for the treatment of solid tumors. Our competitors include, among others:

- companies with approved TIL therapies like Iovance Biotherapeutics, Inc. or those that are developing TIL therapies such as Achilles Therapeutics plc, Instil Bio, Inc., KSQ Therapeutics, Inc., Lyell Immunopharma, Inc., Obsidian Therapeutics, Inc., Intima Bioscience, Inc. and others; and
- companies focused on CAR-T and TCR-T cell therapies for solid-tumors, such as Adaptimmune Therapeutics PLC, Adicet Bio, Inc., Alaunos Therapeutics, Inc., Atara Biotherapeutics, Inc., and Immatics N.V.

In addition, we are aware of other privately held biotechnology companies are evaluating neoantigen directed T cell approaches. Further, there are companies utilizing other cell-based approaches that may be competitive to our product candidates. More effective small molecules, cancer vaccines and other approaches may be developed and used as first line or second line treatments, which would reduce the opportunity for our Selected TIL therapies. Furthermore, we also face competition more broadly across the oncology market for cost-effective and reimbursable cancer treatments.

The most common methods of treating patients with cancer are surgery, radiation, and drug therapy, including chemotherapy, hormone therapy, biologic therapy, such as monoclonal and bispecific antibodies, immunotherapy, cell-based therapy and targeted therapy, or a combination of any such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our Selected TIL product candidates, if any are approved, may compete with these existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our Selected TIL product candidates may not be competitive with them.

Even if we obtain regulatory approval of our product candidates, the availability and price of our competitors' products as well as limits on health insurance reimbursements for our product candidates could limit the demand and the price we are able to charge for our product candidates. We may not be able to implement our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug or biologic products or choose to reserve our product candidates for use in limited circumstances. We believe our ability to successfully compete will depend on our ability to rapidly develop new product candidates, manufacture product supply, successfully enroll patients in clinical trials, gain regulatory approval in target indications, establish collaborations, successfully market and commercialize, and secure and protect intellectual property rights.

Negative developments in the fields of immuno-oncology and TIL-based immunotherapy could damage public perception of our product candidates and adversely affect our business, results of operations and financial condition.

The commercial success of our product candidates will depend in part on public acceptance of the use of cancer immunotherapies and TIL-based immunotherapies. Adverse events in clinical trials of our product candidates or in clinical trials of others developing similar products and the resulting publicity, as well as any other negative developments in the field of immuno-oncology and TIL-based immunotherapy that may occur in the future, could result in a decrease in demand for any product candidates that we may develop. These events also could result in the suspension, discontinuation, or clinical hold of or modification to our clinical trials. If public perception is influenced by claims that the use of cancer immunotherapies and TIL-based immunotherapies is unsafe, whether related to our therapies or those of our competitors, our product candidates may not be accepted by the general public or the medical community and potential clinical trial subjects may be discouraged from enrolling in our clinical trials. As a result, we may not be able to continue or may be delayed in conducting our development programs. For example, administration of certain approved CAR-T therapies has been associated with a risk of secondary malignancies.

Future negative developments in the field of immuno-oncology or the biotechnology industry also could result in greater governmental regulation, stricter labeling requirements and potential regulatory delays in the testing or

approvals of our products. Any increased scrutiny could delay or increase the costs of obtaining marketing approval for any of our product candidates.

Even if a product candidate we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and any revenue that we generate from its sales could be limited.

We have never commercialized a product candidate for any indication. If our current product candidates, including our lead product candidates, or any future product candidate we develop receives marketing approval, whether as a single agent or in combination with other therapies, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, and others in the medical community. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of any of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our products, if approved, for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the ability to obtain sufficient third-party payor coverage and adequate reimbursement; and
- the prevalence and severity of any side effects.

If our product candidates, if approved, do not achieve an adequate level of market acceptance, our business, results of operations and financial condition may be adversely affected.

The size of the potential commercial opportunities for our product candidates is difficult to estimate and, if any of our assumptions are inaccurate, the actual markets for our product candidates may be smaller than our estimates.

The potential commercial opportunities for our product candidates are difficult to estimate and will depend in large part on the drugs with which our product candidates are co-administered and the success of competing therapies and therapeutic approaches. In particular, the commercial opportunity for TIL-based therapies is hard to estimate given that it is an emerging field with no approved TIL therapies. Our estimates of the potential commercial opportunities are predicated on many assumptions, which may include industry knowledge and publications, third-party research reports, and other surveys. The number of patients in the United States and other major markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our product candidates or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our business, results of operations and financial condition. Although we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain, and their reasonableness has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, the actual markets for our product candidates could be smaller than our estimates of the potential commercial opportunities, which could adversely affect our business, results of operations and financial condition.

Risks Related to Our Reliance on Third Parties

We have relied and expect to continue to rely on third parties to conduct certain aspects of our preclinical studies, to conduct our clinical trials and to conduct investigator sponsored clinical trials of our product candidates. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, comply with

regulatory requirements or terminate the relationship, we may not be able to obtain regulatory approval of or commercialize any potential product candidates.

We depend upon on a significant number of third parties, including independent investigators, to conduct certain aspects of our preclinical studies and our clinical trials under agreements with universities, medical institutions, CROs, strategic partners and others. Pursuant to our collaboration agreement with Moffitt, Moffitt's TIDAL-01 IND utilizes product candidate produced by Moffitt, which will be supporting the trial with dedicated cleanroom capacity and manufacturing priority at its on-site facility for TIDAL-01 production. We also utilize CROs to manage certain aspects of our studies, which are conducted at third party clinical sites by third party investigators.

We expect to need to negotiate budgets and contracts with such third parties, which may result in delays to our development timelines and increased costs. We will rely especially heavily on third parties over the course of our clinical trials, and, as a result, will have limited control over and limited visibility into their day-to-day activities, including with respect to their compliance with the clinical protocol. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCP requirements. Upon inspection, such regulatory authorities may determine that any of our clinical trials do not comply with the GCP requirements. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications if at all. In addition, our clinical trials must be conducted with biologic product produced under cGMP or similar foreign requirements and may require a large number of patients, whom we may not be able to recruit.

Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal, state, or foreign fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting aspects of our preclinical studies or our current and future clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties and the ability to enforce them, we cannot control whether or not they devote sufficient time and resources to our preclinical studies and clinical programs. These third parties also may have relationships with other commercial entities, including our competitors, for whom they also may be conducting clinical trials or other product development activities, which could affect their performance on our behalf. 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 preclinical or clinical data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements or for other reasons, our development timelines, including clinical development timelines, may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or other similar organizations expires or is terminated, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms, if at all. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a sometime lengthy transition period when a new CRO begins work. As a result, delays may occur, which can materially impact our ability to meet our desired development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not adversely affect our business, results of operations and financial condition.

Furthermore, we have relied on, and in the future may rely on, separate institutions to conduct and sponsor clinical trials relating to our product candidates. We will not control the design or conduct of the investigator sponsored trials, and it is possible that the FDA or comparable foreign regulatory authorities will not view these

investigator sponsored trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results.

Such arrangements will provide us certain information rights with respect to the investigator sponsored trials, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator sponsored trials. However, we do not have control over the timing and reporting of the data from investigator sponsored trials, nor do we own the data from the investigator sponsored trials. If we are unable to confirm or replicate the results from the investigator sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of our product candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates, or if the data proves to be inadequate compared to the firsthand knowledge we might have gained had the investigator sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected.

Additionally, the FDA or comparable foreign regulatory authorities may disagree with the sufficiency of our right of reference to the preclinical, manufacturing, or clinical data generated by these investigator sponsored trials, or our interpretation of preclinical, manufacturing, or clinical data from these investigator sponsored trials. If so, the FDA or comparable foreign regulatory authorities may require us to obtain and submit additional preclinical, manufacturing, or clinical data before we may initiate our planned trials and/or may not accept such additional data as adequate to initiate our planned trials.

Because we currently rely on third-party manufacturing and supply partners, our supply of research and development, preclinical and clinical development materials may become limited or interrupted or may not be of satisfactory quantity or quality.

We have relied and expect to continue to rely on third-party CDMOs to manufacture some of our preclinical product candidate supplies and to manufacture all of our clinical trial product supplies. Externally, to support TIDAL-01, we have formed deep partnerships across a global network of CDMOs that specialize in bioprocess development, testing, cGMP manufacturing, formulation and filling, packaging, controlled temperature storage, and distribution. For TIDAL-01, this includes a close partnership with the Cell Therapy Facility at Moffitt Cancer Center, responsible for cGMP manufacturing, testing, release, and distribution of Selected TIL to the clinical investigators at Moffitt under our investigator sponsored clinical trial. We have separate partnerships, fully controlled and supervised by us, for the sequencing and peptide manufacturing portions of the TIDAL-01 manufacturing process. In parallel, we have completed a technology transfer of the TIDAL-01 Selected TIL manufacturing process to a U.S.-based CDMO, Charles River Laboratories.

Our preclinical and clinical development product supplies may be limited, interrupted, or not of satisfactory quality or may not continue to be available at acceptable prices. In particular, any replacement of our manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements; this could be particularly problematic where we rely on one CDMO for the manufacture of TIDAL-01. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMP or similar foreign requirements outside the United States. We, or our contract manufacturers, any future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA, competent authorities of EU Member States or other comparable foreign regulatory authorities, to monitor and ensure compliance with cGMP. Despite our efforts to audit and verify regulatory compliance, one or more of our third-party manufacturing vendors may be found on regulatory inspection by the FDA, competent authorities of EU Member States or other comparable foreign regulatory authorities to be noncompliant with cGMP regulations. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including shutdown of the third-party vendor or invalidation of drug product lots or processes, fines, injunctions, civil penalties, delays, suspension, variation or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products, if approved, and significantly harm our business, financial condition, results of operations and prospects.

In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third-party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third-party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third-party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. Moreover, changes to the manufacturer or manufacturing process may be subject to the prior review by the FDA and comparable foreign regulatory authorities, and the FDA and comparable foreign regulatory authorities may not authorize us to utilize product candidates produced by different manufacturers or, if we obtain approval, to commercialize such product produced by different manufacturers than those identified in our marketing applications.

To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, if at all, we may not be able to develop and commercialize our product candidates successfully, if approved. Also, our or a third-party's failure to execute on our manufacturing requirements and comply with cGMPs or similar requirements could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of an existing or future collaborator;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

Failure to maintain cGMPs or similar requirements can result in a contractor receiving FDA or comparable foreign regulatory authorities sanctions, which can impact our ability to operate, obtain or maintain regulatory approvals, or lead to delays in any clinical development programs or future commercialization of any approved products. In addition, any delay in contracting for fill and finish services, or failure of the contract manufacturer to perform the services as needed, may delay any clinical trials, registration and launches, which could adversely affect our business, results of operations and financial condition.

Our current and future collaborations are and will be important to our business. If we are unable to enter into new collaborations, or if these or any of our current collaborations are not successful, our business, results of operations and financial condition could be adversely affected.

A part of our strategy is to strategically evaluate and, as we deem appropriate, enter into additional partnerships in the future, including potentially with major biotechnology or pharmaceutical companies. For example, we entered into a collaboration agreement with Moffitt in connection for the development of TIDAL-01 and an alliance agreement with Moffitt in order to further expand our relationship and support our existing agreements with Moffitt. We have limited capabilities for product development and do not yet have any capability for commercialization. Accordingly, we may continue to enter into collaborations with other companies in the future to provide us with important technologies and funding for our programs and technology.

Our current collaborations and any future collaborations we enter into may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs or license arrangements based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates, if approved;
- collaborators may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- collaborators with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval, if any, may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or future commercialization of product candidates, if approved, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may seek to amend or modify the terms of any collaboration;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or future commercialization of any product candidate licensed to it by us; and
- collaborations may be terminated by the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or future commercialization of the applicable product candidates.

If our collaborations do not result in the successful discovery, development and future commercialization of product candidates, if approved, or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under such collaboration. All of the risks relating to product development, regulatory approval and future commercialization described in this "Risk Factors" section and elsewhere in this Annual Report also apply to the activities of our therapeutic collaborators. Additionally, if one of

our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

We face significant competition in seeking appropriate partners for our product candidates, and the negotiation process is time-consuming and complex. In order for us to successfully partner our product candidates, potential partners must view these product candidates as economically valuable in markets they determine to be attractive in light of the terms that we are seeking and other available products for licensing by other companies. Collaborations are complex, expensive and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Additionally, our collaboration agreements may contain non-competition provisions that could limit our ability to enter into strategic collaborations with future collaborators or restrict our ability to commercialize products on our own, if approved.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization, if approved, or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or future commercialization activities at our own expense. If we elect to increase our expenditures to fund development or future commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms, or at all. If we fail to enter into collaborations or do not have sufficient funds or expertise to undertake the necessary development and future commercialization activities, we may not be able to further develop our product candidates, bring them to market, if approved, and generate revenue from sales of drugs or continue to develop our technology, and our business, results of operations and financial condition could be adversely affected. Even if we are successful in our efforts to establish new strategic partnerships, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic partnerships if, for example, development or approval of a product candidate is delayed or sales of any approved product are disappointing. Any delay in entering into new strategic partnership agreements related to our product candidates could delay the development and future commercialization of our product candidates, if approved, and reduce their competitiveness even if they reach the market.

Our reliance on third parties, such as manufacturers, may subject us to risks relating to manufacturing scale-up and may cause us to undertake substantial obligations, including financial obligations.

As we continue to grow and advance our product candidates through preclinical and clinical trials, we will need to scale our operations accordingly. For example, as we conduct clinical trials of our product candidates, we need to manufacture them in large quantities. We, or any manufacturing partners, may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If we, or any manufacturing partners, are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing, and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could adversely affect our business, results of operations and financial condition.

Risks Related to Government Regulation

The regulatory approval process for our product candidates in the United States and other jurisdictions is currently uncertain and will be lengthy, time-consuming and inherently unpredictable, and we may experience significant delays in the clinical development and regulatory approval, if any, of our product candidates.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products, including biologics like immunotherapies and, cell therapies, are subject to extensive regulation by the FDA in the United States and other regulatory authorities. We are not permitted to market any such products in the United States until we obtain approval of a BLA from the FDA or comparable marketing applications from comparable foreign regulatory authorities. We have not previously submitted a BLA to the FDA, or similar marketing application to comparable foreign authorities. A BLA and similar foreign applications must include

extensive preclinical and clinical data and supporting information to establish that the product candidate is safe, pure and potent (or effective) for each desired indication. A BLA and similar foreign application also must include significant information regarding the chemistry, manufacturing and controls for the product, and the manufacturing facilities must complete a successful pre-license inspection.

The FDA also has the authority to require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, could have a significant impact on our ability to obtain approval of any product candidates that we develop based on the completed clinical trials. Similar decisions may also be taken by foreign regulatory authorities and have similar impact.

In addition, clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- obtaining regulatory authorization to begin a clinical trial, if applicable;
- the availability of financial resources to begin and complete the planned trials;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval at each clinical trial site by an independent IRB or positive ethics committee opinions;
- recruiting suitable patients in sufficient number to participate in a trial in a timely manner;
- having patients complete a trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol, not complying with GCP requirements or dropping out of a trial;
- addressing any patient safety concerns that arise during the course of a clinical trial;
- addressing any conflicts with new or existing laws or regulations;
- our ability to obtain and maintain patient consents;
- adding new clinical trial sites; or
- manufacturing qualified materials under cGMPs or similar regulations for use in clinical trials.

Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors. Further, a clinical trial may be suspended or terminated by us, the IRBs or ethics committees for the institutions in which such trials are being conducted, or the FDA or comparable foreign regulatory authorities, or recommended for suspension or termination by the DSMB for such trial, 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 comparable foreign 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. 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 adversely affected, and our ability to generate product revenue will be delayed or terminated. In addition, any delays in completing any 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.

We may fail to obtain regulatory approval of our product candidates.

The general approach for FDA and equivalent foreign approval of a new biologic is to obtain dispositive data from two well-controlled, Phase 3 clinical trials of the relevant biologic in the relevant patient population. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and take years to complete.

Our clinical trials results may not support approval. In addition, 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 our product candidates are safe and effective for any of their proposed indications;
- 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 our product candidates' clinical and other benefits outweigh their safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of a BLA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- 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 regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

In addition, the FDA and comparable foreign regulatory authorities may change their approval policies and new regulations may be enacted, which could delay or prevent our ability to obtain approval. If any of our product candidates fail to achieve regulatory approval due to the above factors, or otherwise, any such failure would adversely affect our business, results of operations and financial condition.

Our relationships with healthcare providers and physicians and third-party payors may be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of pharmaceutical products. Our current and future arrangements with healthcare providers, third-party payors and customers can expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, which may constrain the business or financial arrangements and relationships through which we research, and if approved, sell, market and distribute our products. In particular, the research of our product candidates, as well as the promotion, sales and marketing of our product candidates is subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. The applicable federal, state and foreign healthcare laws and regulations laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity can be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. The federal 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;

- the federal civil and criminal false claims laws, including the federal False Claims Act or FCA, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal healthcare programs, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or an obligation to pay or transmit money to the federal government, or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government healthcare programs if they are deemed to "cause" the submission of false or fraudulent claims. In addition, 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 FCA. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (*e.g.*, public or private), and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating the health care fraud statute under HIPAA without actual knowledge of the statute or specific intent to violate it;
- the federal Physician Payments Sunshine Act and its implementing regulations, which require some manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the United States Department of Health and Human Services, or HHS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (such as physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback and false claims laws, which may apply to claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and may be broader in scope than their federal equivalents; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and local laws that require the registration of pharmaceutical sales representatives.

Outside the United States, interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such as national anti-bribery laws of European countries, national sunshine rules, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal, state and foreign enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions, significant fines and penalties and settlements in the healthcare industry. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and may divert our management's attention from the operation of our business.

It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from participation in federal and state funded healthcare programs, or comparable foreign programs, contractual damages and the curtailment or restricting of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Any action for violation of these laws, even if successfully defended, could cause us to incur significant legal expenses and divert management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future marketed products could adversely affect our business, results of operations and financial condition.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval of a product candidate, or comparable regulatory authorities in foreign jurisdictions also must approve the manufacturing, marketing and promotion of the product candidate in those jurisdictions. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In some jurisdictions outside the United States a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products also is subject to approval.

We also may submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed, which could adversely affect our business, results of operations and financial condition.

Even if we receive regulatory approval of any product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMPs and similar requirements outside the United States and GCP requirements for any clinical trials that we conduct post-approval.

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 cGMPs or similar regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMPs or similar requirements and adherence to commitments made in any BLA, other marketing application, and previous responses to inspection observations. Accordingly, we and others with which we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may 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 (post-approval) clinical trials and surveillance to monitor the safety and efficacy of the product candidate. The FDA or comparable foreign regulatory authorities may also require a REMS program, or comparable foreign strategies, as a condition of approval of our product candidates or similar risk management measures, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will need to comply with requirements of any such programs including submissions of safety and other post-marketing information and reports and registration.

The FDA or comparable foreign regulatory authorities may impose consent decrees or withdraw or vary 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 our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information or a "black box" warning; 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 or comparable foreign strategies. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA or comparable foreign regulatory authorities to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

Failure to comply with EU and EU Member State laws that apply to the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products and marketing of such products, both before and after grant of the marketing authorization, or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The FDA and comparable foreign regulatory authorities strictly regulate marketing, labeling, advertising, and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and comparable foreign regulatory authorities 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 civil, criminal and administrative liability. The policies of the FDA and comparable 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 action, either in the United States or abroad. 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 our business, results of operations and financial condition could be adversely affected. For example, on April 26, 2023, the European Commission adopted a proposal for a new Directive and Regulation to revise the existing pharmaceutical legislation. If adopted in the form proposed, the recent European Commission proposals to revise the existing EU laws governing authorization of medicinal products may result in a decrease in data and market exclusivity opportunities for our product candidates in the EU and make them open to generic or biosimilar competition earlier than is currently the case with a related reduction in reimbursement status.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, if approved, which could make it difficult for us to sell any product candidates profitably.

The success of our product candidates, if approved, depends on the availability of coverage and adequate reimbursement from third-party payors. We cannot be certain that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will continue to be available for any product that we may develop that receives coverage and adequate reimbursement from one or more third-party payors. Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Accordingly, coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of product candidates. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates. In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. 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 Medicare, review the relationship between pricing and

manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to President Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. 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 expect to experience pricing pressures in connection with the sale of all of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes.

Ongoing healthcare legislative and regulatory reform measures may adversely affect our business, results of operations and financial condition.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (1) changes to our manufacturing arrangements; (2) additions or modifications to product labeling; (3) the recall or discontinuation of our products; (4) post-marketing approvals or compliance programs or (5) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect our business, results of operations and financial condition.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, was passed by Congress, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, subjected biological products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers 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.

Since its enactment, certain provisions of the ACA have been subject to executive, judicial and congressional challenges. On June 17, 2021, the U.S. Supreme Court dismissed the most recent challenge to the ACA on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, President Biden issued an executive order that initiated 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 instructed certain governmental authorities 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. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or 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 and through a newly established manufacturer discount program. It is unclear how other healthcare reform measures of the Biden administration, if any, will impact our business.

Other legislative changes have 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 of Medicare

payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013, and, due to subsequent legislative amendments, will stay in effect through 2032 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Further, 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. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. It is currently unclear how the IRA will be implemented but it is likely to have a significant effect on the pharmaceutical industry. In response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the Centers for Medicare & Medicaid Services, or CMS, Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework.

These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

EU drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for our products in the EU member states.

We intend to seek approval to market our product candidates in the United States and we may also seek to do so in selected foreign jurisdictions, including the EU. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of medicinal products is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. Some countries provide that products may be marketed only after a reimbursement decision has been taken by the relevant regulatory authority. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future health care reform measures.

Payments made to physicians and healthcare organizations in certain EU member states must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and/or approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU member states. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

In addition, in most foreign countries, including the EU, the requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced EU member states, can further reduce prices.

An EU member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Many EU Member States also periodically review their reimbursement procedures for medicinal products, which could have an adverse impact on reimbursement status. In some countries, we may also be required to conduct a clinical study or other studies that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. This Health Technology Assessment ("HTA") of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including those representing the larger markets. The HTA process is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU Member States. In December 2021, Regulation No. 2021/2282 on Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted. This regulation which will apply from January 12, 2025 intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation foresees a three-year transitional period and will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement.

There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales by us or our strategic partners and the potential profitability of any of our product candidates in those countries would be negatively affected.

Disruptions at the FDA and other national and foreign government and regulatory authorities caused by funding shortages or global health concerns, such as COVID-19, 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 and comparable foreign regulatory authorities 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 and foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's and comparable foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and comparable foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government authorities that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other national and foreign authorities also may slow the time necessary for new biologics or modifications to approved biologics to be reviewed and/or approved by necessary government authorities, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory authorities, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

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.

Our product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. 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 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 the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

There is a risk that any of our product candidates approved as a biological product under a BLA would not qualify for the 12-year period of exclusivity or that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. If competitors are able to obtain marketing approval for biosimilars referencing our candidates, if approved, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information, such as information that we may collect in connection with clinical trials. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulations, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our business, results of operation, and financial condition.

We may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the United States, HIPAA as amended by the Health Information Technology for Economic and Clinical Health Act, or collectively, HIPAA, imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly regulated under HIPAA, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information.

Certain states have also adopted comparable privacy and security laws and regulations. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, the California Consumer Privacy Act of 2018, or CCPA, went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the California Privacy Rights

Act, or CPRA, generally went into effect on January 1, 2023 and significantly amends the CCPA and imposes 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 also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. Similar laws have passed in Virginia, Colorado, Utah, Iowa and Connecticut and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

We are also or may become subject to rapidly evolving data protection laws, rules and regulations in foreign jurisdictions. For example, in Europe, the EU and the UK General Data Protection Regulations (respectively, the EU GDPR and UK GDPR; together, the GDPR) each impose strict requirements for processing the personal data of individuals within the European Economic Area, or EEA, and/or the UK. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million under the EU GDPR and £17.5 million under the UK GDPR or 4% of the annual global revenues of the noncompliant company, whichever is greater. In addition to these fines, supervisory authorities have extensive audit and inspection rights, and powers to order temporary or permanent bans on all or some processing of personal data carried out by noncompliant actors; the GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. We could be subject to potentially overlapping or divergent enforcement actions for certain actual or perceived violations. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States. In July 2020, the Court of Justice of the EU, or CJEU, limited how organizations could lawfully transfer personal data from the EU/EEA to the United States by invalidating the Privacy Shield for purposes of international transfers. To facilitate such transfers a new set of standard contractual clauses, or SCCs, was issued by the European Commission but these apply only to transfers of personal data outside the EEA under the EU GDPR. Organizations are now required to comply with onerous obligations to determine the additional measures that need to be implemented and maintained to supplement such safeguards to protect the transferred personal data effectively. In March 2022, the US and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU-US Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for United States Signals Intelligence Activities. European court and regulatory decisions subsequent to the CJEU decision of July 2020 have taken a restrictive approach to international data transfers. As supervisory authorities issue further guidance on personal data export mechanisms, 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. The GDPR may impose additional responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms, at significant cost and diversion of management attention, to ensure compliance with the new data protection rules. This may be onerous and adversely affect our business, results of operations and financial condition.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

Additional laws and regulations governing international operations could adversely affect our business, results of operations and financial condition.

If we further expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or the FCPA prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate and other related parties 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 certain accounting provisions requiring the company 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.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our research and development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The U.S. Securities and Exchange Commission, or the SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations.

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government authorities or government-affiliated hospitals, universities, and other organizations. We also expect our non-U.S. activities to increase over time. We plan to engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals, and we can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

Risks Related to Our Intellectual Property

Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.

As of December 31, 2023, we own or exclusively license 11 issued U.S. patents and 78 issued foreign patents in 19 countries. We currently own or exclusively license 17 pending U.S. patent applications, three U.S. provisional applications, two pending international PCT applications, and 74 pending foreign patent applications in 11 other countries. Our commercial success will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties

from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities. If we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop may be adversely affected.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications in all jurisdictions at a reasonable cost or in a timely manner. Moreover, obtaining such protection in a timely manner, or at all, may be affected by factors or events beyond our control, such as a prolonged economic downturn, or global financial or political crises, or the ongoing political unrest between Russia and the Ukraine. In addition, we may not pursue or obtain patent protection in all relevant markets. It also is possible that we will fail to identify and file on patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such results before a patent application is filed, thereby jeopardizing our ability to seek patent protection. If we delay in filing a patent application, and a competitor files a patent application on the same or a similar technology before we do, we may face a limited ability to secure patent rights. Or we may not be able obtain a patent on such technology at all. Even if we can patent the technology, we may be able to patent only a limited scope of the technology, and the limited scope may be inadequate to protect our product candidates, or to block competitor products or product candidates that are similar to ours. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees.

Composition of matter patents for biological and pharmaceutical product candidates often provide a strong form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. Method of use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products “off-label.” Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

Certain of our programs may involve combination therapies. Composition of matter and method of use patents directed to combination therapies may be subject to heightened patentability standards and, therefore, may be difficult to issue worldwide.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced.

Since patent applications in the United States and most other countries are confidential for a period of time after filing, we may not have been the first to file any patent application related to our product candidates. Furthermore, for United States applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the United States patent office, or

USPTO, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

We may not be the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, a competitor's technology or product would be found by a court to infringe our patents. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidates or our activities infringing such claims. The possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights, or will design around the claims of patents that we have had issued that cover our products.

Recent or future changes in patent-related case law and/or patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. For example, under the enacted Leahy-Smith America Invents Act, or America Invents Act, enacted in 2013, the United States moved from a "first to invent" to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear as the USPTO only recently developed new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the "first-to-file" provisions, became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Recent changes in European law have caused uncertainty regarding our European patent portfolios. In particular, in 2012, the European Patent Package, or EU Patent Package, regulations were passed with the goal of providing for a single pan-European Unitary Patent, and a new European Unified Patent Court, or UPC, for litigation of European patents. The EU Patent Package was ratified in February 2023 and currently covers 17 member states. On June 1, 2023, all European patents, including those issued prior to ratification, will by default automatically fall under the jurisdiction of the UPC and allow for the possibility of obtaining pan-European injunctions, and further will be at risk of a central revocation proceeding at the UPC in participating UPC states. Under the EU Patent Package, patent holders are permitted to "opt-out" of the UPC on a patent-by-patent basis during an initial seven-year period after the EU Patent Package is ratified, with the proviso that an "opt-out" is no longer available for EP patents for which a revocation has been initiated before the UPC. Owners of European patent applications who receive notice of grant after the EU Patent Package is ratified could, for the UPC contracting states, either obtain a Unitary Patent or validate the patent nationally and file an opt-out demand. The EU Patent Package may increase the uncertainties and costs surrounding the enforcement or defense of our issued European patents and pending applications. The full impact on future European patent filing strategy and the enforcement or defense of our issued European patents in member states and/or the UPC is not known.

Intellectual property rights do not necessarily address all potential threats to our business.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds or cells that are similar to the biological compositions of our product candidates but that are not covered by the claims of our patents;
- the active biological ingredients in our current product candidates will eventually become commercially available in biosimilar drug products, and no patent protection may be available with regard to formulation or method of use;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- we or our licensors, as the case may be, might not have been the first to file patent applications for the inventions we own or control;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that a court could find the disclosure of our owned or -in-licensed patents is not sufficient to support the scope of issued claims, thereby invalidating the claims;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns;
- our competitors might conduct research and development activities in the United States and other foreign countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights and then use the information learned from such activities to develop competitive product candidates for sale in our major commercial markets;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- we may need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;

- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- we have engaged in scientific collaborations in the past, and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on our business, including if others obtain patents claiming subject matter similar to or improving that covered by our patents and patent applications.

Any difficulties we encounter in defending, or resulting inability to protect, our proprietary rights and technology, may adversely affect our business, results of operations and financial condition.

We depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which could adversely affect our business, results of operations and financial condition.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others. Any termination of these licenses could result in the loss of significant rights and could harm our ability to commercialize our product candidates.

Disputes also may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes 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;
- the priority of invention of patented technology;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and future commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of and rights to use inventions and know-how resulting from the joint or individual creation or use of intellectual property by our licensors and us and our partners.

In addition, certain of our current and future agreements with third parties may limit or delay our ability to consummate certain transactions, may impact the value of those transactions, or may limit our ability to pursue certain activities. For example, we may enter into license agreements that are not assignable or transferable, or that require the licensor's express consent in order for an assignment or transfer to take place. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We generally also are subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described in this "Risk Factors" section. If we or our licensors fail to adequately protect this intellectual property, our business, results of operations and financial condition could be adversely affected.

If we fail to comply with our obligations under our patent licenses with third parties, we could lose license rights that are important to our business, which could adversely affect our business, results of operations and financial condition.

We are a party to license agreements pursuant to which we in-license patent and patent applications, know-how, trade secrets and data rights for our product candidates. These existing licenses impose on us various diligence, milestone payment, royalty, insurance and other obligations. If we fail to comply with these obligations, our licensors may have the right to terminate the license, in which event we would not be able to develop or market the products covered by such licensed intellectual property.

Our licensors retain certain rights under their agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse.

We may also enter into license agreements with third parties under which we are a sublicensee. If our sublicensor fails to comply with its obligations under its upstream license agreement with its licensor, the licensor may have the right to terminate the upstream license, which may terminate our sublicense. If this were to occur, we would no longer have rights to the applicable intellectual property unless we are able to secure our own direct license with the owner of the relevant rights, which we may not be able to do on reasonable terms, or at all, which may impact our ability to continue to develop and commercialize our product candidates incorporating the relevant intellectual property.

We may have limited control over the maintenance and prosecution of these in-licensed patents and patent applications, activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, such activities by these licensors may not have been or may not be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. Our licensors may not successfully prosecute the patent applications to which we are licensed in a manner consistent with the best interests of our business. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves.

If we are unable to protect the confidentiality of our trade secrets, our business, results of operations and financial condition could be adversely affected.

In addition to patent and other intellectual property protection, we rely heavily upon know-how and trade secret protection, as well as non-disclosure agreements and invention assignment agreements with our employees, consultants and third parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable. Elements of our product candidates, including processes for their preparation and manufacture, may involve proprietary know-how, information, or technology that is not covered by patents and that may not be patentable, and thus for these aspects we may consider trade secrets and know-how to be our primary intellectual property. We may also rely on trade secret protection as temporary protection for concepts that may be included in a future patent filing. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not, for example, in the case of misappropriation of a trade secret by an employee or third-party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may be expensive and not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, trade secrets may be independently developed by others in a manner that could prevent legal recourse by us. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed.

In addition, courts outside the United States are sometimes less willing to protect trade secrets. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. If we choose to go to court to stop a third-party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees, consultants and current and potential business partners, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology.

Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors and current and potential business partners to execute confidentiality agreements upon the commencement of employment, consulting or other applicable relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. Any disclosure, either intentional or unintentional, by our employees or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Because we expect to rely on third parties in the development and manufacture of our product candidates, we must, at times, share trade secrets with them, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our sole and exclusive property. We also have adopted policies and conduct training that provides guidance on our expectations, and our advice for best practices, in protecting our trade secrets.

We cannot prevent other companies from licensing some of the same intellectual properties that we have licensed or from otherwise duplicating our business model and operations.

Since parties we have licenses with are developing therapies to similar technologies, they may make their methods and data available to third parties, who may want to enter into our line of business and compete against us. We currently do not have any exclusive rights to our entire product portfolio that could be used to prevent third parties from duplicating our business plan or from otherwise directly competing against us. No assurance can be given that our existing exclusive rights are or will be sufficient to prevent others from competing with us and developing substantially similar products.

Third-party claims of intellectual property infringement may prevent or delay our product discovery and development efforts.

Our commercial success depends in part on our ability to research, develop, manufacture, market and sell our current and any future product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. We are further aware of certain patents, and patent applications in the United States and elsewhere that contain claims that, if issued in their present form, may cover our TIL products or their methods of use or manufacture. We, along with a number of third parties in the TIL cell therapy field, have been involved in opposition proceedings in Europe with respect to some of these patents. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or

manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

If a third-party claims that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third-party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third-party licenses its product rights to us, which it is not required to do;
- if a license is available from such third-party (and no such license may be available), we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products; and
- redesigning our product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise adversely affect our business, results of operations and financial condition.

Third parties may assert that we are employing their proprietary technology without authorization. Generally, conducting clinical trials and other development activities in the United States is protected under the Safe Harbor exemption as set forth in 35 U.S.C. § 271. If and when one of our product candidates is approved by the FDA, that certain third-party may then seek to enforce its patent by filing against us a patent infringement lawsuit. In this regard, patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is "clear and convincing," a heightened standard of proof. There may be third-party patents of which we currently are unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. We have conducted freedom to operate analyses with respect to only certain of our products and services and we cannot guarantee that our analyses are complete and thorough, nor can we be sure that we have identified each and every patent and pending application in the United States and abroad that is relevant or necessary to the commercialization of our products and services. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe.

In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, constructs or molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent 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. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same

technologies licensed to us. 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.

In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our business, results of operations and financial condition.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. In addition, if our product candidates are found to infringe the intellectual property rights of third parties, these third parties may also assert infringement claims against our licensees and other parties with whom we have business relationships, and we may be required to indemnify those parties for any damages they suffer as a result of these claims. If any of these claims succeed, we may be required to pay damages on behalf of those parties or may be required to obtain licenses for the products they use. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. Any such license may not be available at all or may not be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow future commercialization of our product candidates, if approved. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could adversely affect our business, results of operations and financial condition.

Third parties may assert that our employees, consultants or other third parties have wrongfully used, disclosed confidential information, misappropriated trade secrets or are in breach of non-competition or non-solicitation agreements.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at universities or other biopharmaceutical or pharmaceutical companies, including our competitors or potential competitors. Although no material claims against us currently are pending or threatened, and although we try to ensure that our employees, consultants and other third parties do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants, independent contractors or current or potential business partners have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties, or are in breach of any non-competition or non-solicitation agreements. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities.

We may 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. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. 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. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. 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, valuable intellectual property.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, results of operations and financial condition.

In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our business, results of operations and financial condition.

We may not be successful in obtaining or maintaining necessary rights to develop current and any future product candidates on acceptable terms.

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 may depend in part on our ability to acquire, in-license or use these proprietary rights.

Our product candidates also may require specific formulations 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 as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and expenses and development delays, even if we were able to develop such alternatives, which may not be feasible. 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.

Additionally, we sometimes collaborate with academic institutions and governmental authorities to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business, results of operations and financial condition could be adversely affected.

The licensing and acquisition of third-party intellectual property rights is a highly competitive area, and companies, which may be more established, or have greater resources than we do, also may be pursuing strategies to

license or acquire third-party intellectual property rights that we 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. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or insufficient written description. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. For the patents and patent applications that we have licensed, we may have limited or no right to participate in the defense of any licensed patents against challenge by a third party. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future product candidates. Such a loss of patent protection could harm our business.

In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable, or 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. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. Moreover, our ability to successfully pursue infringement claims or otherwise enforce intellectual property that we license from or co-own with another party may require the participation and co-operation of the co-owner or licensor, and may be impaired or prohibited if such participation or co-operation is insufficient or cannot be secured.

We may choose to challenge the patentability of claims in a third-party's U.S. patent by requesting that the USPTO review the patent claims in an *ex-parte* re-exam, *inter partes* review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third-party's patent in patent opposition proceedings in the European Patent Office, or EPO, or another foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third-party alleging that the patent may be infringed by our product candidates or proprietary technologies.

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, others may have filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, and we or, if applicable, a licensor may not have been the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our owned and in-licensed patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. For applications that have claims entitled to a priority date before March 16, 2013, if another party has filed a U.S. patent application on inventions similar to those owned by or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the United States. If we or one of our licensors is a party to an interference proceeding involving a U.S. patent application on inventions owned by or in-licensed to us, we may incur substantial costs, divert management's time and expend other resources, even if we are successful.

Interference proceedings provoked by third parties or brought by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology 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 a license on commercially reasonable terms. Litigation or interference proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States.

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. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees, and various other governmental fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process and following the issuance of a patent. 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 loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which could adversely affect our business, results of operations and financial condition.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO.

If we or one of our licensing partners initiate legal proceedings against a third-party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third-party can assert invalidity or unenforceability of a patent. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post grant review, derivation proceedings and equivalent proceedings in foreign jurisdictions (*e.g.*, opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, there may be 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 invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could adversely affect our business, results of operations and financial condition.

Changes in patent law in the United States and in other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both

technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has enacted and is currently implementing the America Invents Act. Moreover, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in other situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, in the case of *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.,* the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. We cannot predict how these decisions or any future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents. Similarly, any adverse changes in the patent laws of other jurisdictions could adversely affect our business, results of operations and financial condition.

We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.

We have limited intellectual property rights outside the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can have a different scope and strength than those in the United States. Moreover, obtaining such protection in a timely manner, or at all, may be affected by factors or events beyond our control, such as a prolonged economic downturn, or global financial or political crises, whether or not related to the ongoing political unrest between Russia and the Ukraine and between Israel and Hamas. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from 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, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally. The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Proceedings to enforce our patent and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Similarly, if our trade secrets are disclosed in a foreign jurisdiction, competitors worldwide could have access to our proprietary information and we may be without satisfactory recourse. Such disclosure could have a material adverse effect on our business. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. In addition, certain countries, including China and India, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. In addition, many countries limit the enforceability of patents against government authorities or government contractors. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

We may incur substantial costs as a result of litigation or other proceedings relating to patents, and we may be unable to protect our rights to our products and technology.

If we or our licensors choose to go to court to stop a third-party from using the inventions claimed in our owned or in-licensed patents, that third-party may ask the court to rule that the patents are invalid and/or should not be enforced against that third-party. These lawsuits are expensive and would consume time and other resources even if we or they, as the case may be, were successful in stopping the infringement of these patents. In addition, there is a risk that the court will decide that these patents are not valid and that we or they, as the case may be, do not have the right to stop others from using the inventions. An adverse determination in any such proceeding could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us. An unfavorable result at the USPTO, EPO or other patent office may result in the loss of our right to exclude others from practicing one or more of our inventions in the relevant country or jurisdiction, which could adversely affect our business, results of operations and financial condition.

There also is the risk that, even if the validity of these patents is upheld, the court will refuse to stop the third-party on the ground that such third-party's activities do not infringe our owned or in-licensed patents. In addition, the U.S. Supreme Court recently has changed some legal principles that affect patent applications, granted patents and assessment of the eligibility or validity of these patents. As a consequence, issued patents may be found to contain invalid claims according to the newly revised eligibility and validity standards. Some of our owned or in-licensed patents may be subject to challenge and subsequent invalidation or significant narrowing of claim scope in proceedings before the USPTO, or during litigation, under the revised criteria which also could make it more difficult to obtain patents.

We, or our licensors, may not be able to detect infringement against our owned or in-licensed patents, as the case may be, which may be especially difficult for manufacturing processes or formulation patents. Even if we or our licensors detect infringement by a third-party of our owned or in-licensed patents, we or our licensors, as the case may be, may choose not to pursue litigation against or settlement with the third-party. If we, or our licensors, later sue such third-party for patent infringement, the third-party may have certain legal defenses available to it, which otherwise would not be available except for the delay between when the infringement was first detected and when the suit was brought. Such legal defenses may make it impossible for us or our licensors to enforce our owned or in-licensed patents, as the case may be, against such third-party.

If another party questions the patentability of any of our claims in our owned or in-licensed U.S. patents, the third-party can request that the USPTO review the patent claims such as in an *inter partes* review, *ex parte* re-exam or post-grant review proceedings. These proceedings are expensive and may result in a loss of scope of some claims or a loss of the entire patent. In addition to potential USPTO review proceedings, we may become a party to patent opposition proceedings at the EPO or similar proceedings in other foreign patent offices, where either our owned or in-licensed foreign patents are challenged.

In the future, we may be involved in similar proceedings challenging the patent rights of others, and the outcome of such proceedings is highly uncertain.

An adverse determination in any such proceeding may result in our inability to manufacture or commercialize products without infringing third-party patent rights. The costs of these opposition or similar proceedings could be substantial, and may result in a loss of scope of some claims or a loss of the entire patent.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional application filing date. Various extensions such as patent term adjustments and/or extensions, may be available, but the life of a patent, and the protection it affords, is limited. For instance, a patent term extension based on regulatory delay may be available in the United States. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the patent term extension does not necessarily extend to all claims, but instead only to claims that cover the product as approved. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including biosimilars. Given the amount of time required for the

development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

As of December 31, 2023, we own or in-license patent applications covering our proprietary technologies and our product candidates that if issued as patents are expected to expire between 2039 and 2044, without taking into account any possible patent term adjustments or extensions. However, the USPTO or relevant foreign patent offices may not grant any of these patent applications. If issued, the patents may expire before, or soon after, our first product achieves marketing approval in the United States or foreign jurisdictions. Further, if issued, the patents may expire before, or soon after, any regulatory protection afforded our first approved product through data and/or market exclusivity in the United States or foreign jurisdictions. Upon the expiration of any such patents, if issued, we may lose the right to exclude others from practicing these inventions. The expiration of these patents also could adversely affect our business, results of operations and financial condition.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business, results of operations and financial condition could be adversely affected.

Our trademarks or trade names may be challenged, opposed, infringed, circumvented, invalidated, cancelled, declared generic, determined not to entitled to registration, or determined to be infringing on other marks. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in foreign jurisdictions. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Any trademark litigation could be expensive. In addition, we could be found liable for significant monetary damages, including treble damages, disgorgement of profits and attorneys' fees, if we are found to have willfully infringed a trademark.

Moreover, any name we propose to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark.

We may not be able to protect our rights to our trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business, results of operations and financial condition could be adversely affected.

Risks Related to Our Common Stock

The price of our common stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K, these factors include:

- the progress, conduct, enrollment or results of our two Phase 1 clinical trials for TIDAL-01;

- any termination of, loss of rights or disputes or disagreements arising under our collaboration, partnership and strategic alliance agreements;
- any delay in identifying additional product candidates from our current and future development programs;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings;
- adverse results or delays in future clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval of our current product candidates or any future product candidate;
- changes in laws or regulations applicable to our current product candidates or any future product candidate, including but not limited to clinical trial requirements for approvals;
- adverse development concerning our competitors, particularly those developing TIL-based therapies;
- adverse developments concerning our manufacturers;
- adverse developments concerning our manufacturing process, including manufacturing failures;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- our inability to establish collaborations or other strategic relationships, if needed;
- our ability to successfully develop and the costs associated with the development of our internal manufacturing processes;
- our failure to commercialize our product candidates, if approved;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of our current product candidates or any future product candidate;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or our or a competitor's product candidates in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- volatility and instability in the financial and capital markets;
- overall performance of the equity markets, including the effects of geopolitical events;
- sales of our common stock by us, our insiders, or other stockholders in the future, or issuances by us of shares of our common stock in connection with strategic transactions;

- expiration of market standoff or lock-up agreements described in the section titled "Underwriting";
- conditions and trends in the biotechnology and other industries;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to intellectual property and other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- changes in the structure of healthcare payment systems, including coverage and adequate reimbursement for any approved drug;
- global or regional public health emergencies, including pandemics, natural disasters, or major catastrophic events;
- adverse macroeconomic conditions or geopolitical events, including the conflict between Ukraine and Russia, the conflict in the Middle East, and recent bank failures;
- the occurrence of any of the risks described in this section titled "Risk Factors"; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that often have been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation often has been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which could adversely affect our business, results of operations and financial condition.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the research, development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any future debt or other financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders therefore will be limited to the appreciation of the price of our common stock.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of December 31, 2023, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially held, in the aggregate, approximately 51.0% of our outstanding common stock. These stockholders, acting together, would be able to significantly influence all matters requiring stockholder approval. For example, these stockholders would be able to significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This level of control may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

We are an emerging growth company and a smaller reporting company, and the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We will remain an emerging growth company until the earlier of (1) (a) December 31, 2027, (b) the last day of the fiscal year in which we have total annual gross revenue of at least $1.235 billion and (c) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700.0 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. Investors may find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies also can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to avail ourselves of this exemption, and, as a result, our operating results and financial statements may not be comparable to the operating results and financial statements of companies who have adopted the new or revised accounting standards.

We also are a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than $700.0 million and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We will continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our annual report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Conflicts of interest may arise because some members of our board of directors are representatives of our principal stockholders.

Certain of our principal stockholders or their affiliates are venture capital funds or other investment vehicles that could invest in entities that directly or indirectly compete with us. As a result of these relationships, when conflicts arise between the interests of the principal stockholders or their affiliates and the interests of other stockholders, members of our board of directors that are representatives of the principal stockholders may not be disinterested.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If our stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our existing equity compensation plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, future lock-up agreements and Rule 144 under the Securities Act of 1933, as amended, or the Securities Act and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Certain holders of approximately 13.3 million shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act as provided under the terms of the Second Amended and Restated Investors' Rights Agreement, or the Rights Agreement, between us and the certain of our stockholders, or the Myst Merger Agreement, Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of our company more difficult, limit attempts by our stockholders to replace or remove our current management and limit the market price of our common stock.

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may have the effect of delaying or preventing a change of control or changes in our board of directors and management. Our amended and restated certificate of incorporation and amended and restated bylaws include provisions that:

- authorize our board of directors to issue, without further action by the stockholders, shares of undesignated preferred stock with terms, rights and preferences determined by our board of directors that may be senior to our common stock;
- require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;
- specify that special meetings of our stockholders can be called only by directors representing a majority of the total authorized size of our board of directors, the chairperson of our board of directors, our chief executive officer or our president;
- establish an advance notice procedure for stockholder proposals to be brought before an annual meeting, including proposed nominations of persons for election to our board of directors;
- establish that our board of directors is divided into three classes, with each class serving three-year staggered terms;
- prohibit cumulative voting in the election of directors, therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose;
- provide that our directors may be removed for cause only upon the vote of at least 66 2/3% of our outstanding shares of voting stock;
- 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; and
- require the approval of our board of directors or the holders of at least 66 2/3% of our outstanding shares of voting stock to amend our bylaws and certain provisions of our certificate of incorporation.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or DGCL, which generally, subject to certain exceptions, prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any "interested" stockholder for a period of three years following the date on which the stockholder became an "interested" stockholder. Any of the foregoing provisions could limit the price that investors might be willing to pay in the future for shares of our common stock, and they could deter potential acquirers of our company, thereby reducing the likelihood that holders of our common stock would receive a premium for their shares of our common stock in an acquisition.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district court for the District of Delaware of the United States will be the exclusive

forums 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 the Court of Chancery of the State of Delaware is 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 breach of fiduciary duty;
- any action asserting a claim against us arising under the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws;
- any action seeking to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation, or our amended and restated bylaws;
- any action to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. 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 further provides that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid and several state trial courts have enforced such provisions and required that suits asserting Securities Act claims be filed in federal court, there is no guarantee that courts of appeal will affirm the enforceability of such provisions and a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and the provisions may not be enforced by a court in those other jurisdictions. This exclusive forum provision may result in increased costs to stockholders to bring a claim. Further, this exclusive forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with litigating Securities Act claims in state court, or both state and federal court, which could seriously harm our business, results of operations and financial condition.

General Risk Factors

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will incur significant legal, accounting, compliance and other expenses that we did not incur as a private company. We will be subject to the reporting requirements of the Exchange Act, which will require, among other things, that we file with the SEC annual, quarterly, and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Emerging growth companies and smaller reporting companies are exempted from certain of these requirements, but we may be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, results of operations and financial condition. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements also makes it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

We are not currently required to comply with the rules of the SEC implementing Section 404 of the Sarbanes-Oxley Act and are therefore not required to make a formal assessment of the effectiveness of our internal control over financial reporting for that purpose. Upon becoming a public company, we will be required to comply with the SEC's rules implementing Sections 302 and 404 of the Sarbanes-Oxley Act, which will require management to certify financial and other information in our quarterly and annual reports and provide an annual management report on the effectiveness of internal control over financial reporting. Although we will be required to disclose changes made in our internal control over financial reporting on a quarterly basis, we will not be required to make our first annual assessment of our internal control over financial reporting until our second annual report on Form 10-K. However, as an emerging growth company, our independent registered public accounting firm will not be required to formally attest to the effectiveness of our internal control over financial reporting until the later of the year following our first annual report required to be filed with the SEC or the date we are no longer an emerging growth company. When we lose our status as an "emerging growth company" and reach an accelerated filer threshold, 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 our 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 may need to upgrade our information technology systems; implement additional financial and management controls, reporting systems and procedures; and hire additional accounting and finance staff. If we or, if required, our auditors are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

There may be 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 once that firm begins its Section 404 reviews, 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 Nasdaq, 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 must design our disclosure controls and procedures 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. Any disclosure 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 any related party transaction disclosures. 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. In addition, we do not have a formal risk management program for identifying and addressing risks to our business in other areas.

We could be subject to securities class action litigation, which is expensive and could divert management attention.

The market price of our common stock is likely to be volatile. The stock market in general, and Nasdaq and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of companies. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs (including the cost to defend against, and any potential adverse outcome resulting from any such proceeding), damage to our reputation, and a diversion of management's attention and resources from other business concerns, which could harm our business.

Our failure to meet Nasdaq's continued listing requirements could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of Nasdaq, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with the listing requirements of Nasdaq.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company, the trading price for our stock would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which would likely cause our stock price and trading volume to decline.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 1C. Cybersecurity

Risk management and strategy

We have implemented and maintain various information security processes designed to identify, assess and manage material risks from cybersecurity threats to our critical computer networks, third party hosted services, communications systems, hardware and software, and our critical data, including intellectual property, confidential information that is proprietary, strategic or competitive in nature, and trade secrets, data we may collect about trial participants in connection with clinical trials, sensitive third-party data, business plans, transactions, and financial information ("Information Systems and Data").

Our IT, legal, and finance departments work with the information security function within the Company to help identify, assess and manage the Company's cybersecurity threats and risks. Our information security function identifies and assesses risks from cybersecurity threats by monitoring and evaluating our threat environment using various methods including, for example, automated tools, internal or external audits, subscribing to and analyzing reports and intelligence feeds that identify cybersecurity threats and threat actors, conducting threat assessments (both internally and by third parties) for internal and external threats, evaluating our and our industry's risk profile, conducting vulnerability assessments to identify vulnerabilities, conducting scans of the threat environment, coordinating with law enforcement concerning threats, and evaluating threats reported to us. Depending on the environment, we implement and maintain various technical, physical, and organizational measures, processes, standards and policies designed to manage and mitigate material risks from cybersecurity threats to our Information Systems and Data, including, for example: incident detection and response, data encryption, network security controls, data segregation, asset management, tracking, and disposal, access controls, system monitoring, employee training, disaster recovery/business continuity plans, risk assessments, implementation of security standards/certifications, cyber insurance, and physical security mechanisms.

Our assessment and management of material risks from cybersecurity threats are integrated into the Company's overall risk management processes. For example, the information security function works with management to prioritize our risk management processes and mitigate cybersecurity threats that are more likely to lead to a material impact to our business.

We use third-party service providers to assist us from time to time to identify, assess, and manage material risks from cybersecurity threats, including for example professional services firms (including legal counsel), threat intelligence service providers, cybersecurity consultants, cybersecurity software providers.

We also use third-party service providers to perform a variety of functions throughout our business, such as application providers, hosting companies, contract research organizations, contract manufacturing organizations, and supply chain resources. We manage cybersecurity risks associated with our use of these providers by reviewing their security assessments, reviewing their written security program, and applicable reports.

For a description of the risks from cybersecurity threats that may materially affect the Company and how they may do so, see our risk factors under Part 1. Item 1A. Risk Factors in this Annual Report on Form 10-K, including "Our internal information technology systems, or those of our third-party contract research organizations, contract manufacturing organizations and other contractors and consultants, may fail or suffer security breaches, loss or leakage of data and other disruptions, which could result in a material disruption of our development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability, and could adversely affect our business, results of operations and financial condition".

Governance

Our board of directors addresses the Company's cybersecurity risk management as part of its general oversight function. The audit committee within the board of directors' is responsible for overseeing Company's cybersecurity risk management processes, including oversight and mitigation of risks from cybersecurity threats.

Our cybersecurity risk assessment and management processes are implemented and maintained by certain Company management, including our IT Director, who has over 24 years of IT management experience for public companies including Synergy Pharmaceuticals, Inc.

Our information security function is responsible for hiring appropriate personnel, helping to integrate cybersecurity risk considerations into the Company's overall risk management strategy, and communicating key priorities to relevant personnel. Our CFO and information security function are responsible for approving budgets, helping prepare for cybersecurity incidents, approving cybersecurity processes, and reviewing security assessments and other security-related reports.

Our response process to cybersecurity incidents is designed to escalate certain incidents to members of management depending on the circumstances, including the CFO. Our CFO and others work with the Company's incident response team to help the Company mitigate and remediate cybersecurity incidents of which they are notified. In addition, the Company's incident response policy includes reporting to the board of directors committee responsible for certain cybersecurity incidents.

The board committee receives periodic reports from our information security function (including our IT Director) concerning the Company's significant cybersecurity threats and risk and the processes the Company has implemented to address them. The board committee also has access to various reports, summaries or presentations related to cybersecurity threats, risk and mitigation.

Item 2. Properties.

In July 2018, the Company entered into a lease agreement for approximately 6,500 square feet of office space in New York, New York. The Company subleased this space in November, 2022 until the lease expires in February 2026.

In May 2019, the Company entered into a lease for approximately 9,423 square feet located in Ottawa, Ontario, Canada. The lease expires in November 2024.

In June 2021, the Company leased its current corporate headquarters of approximately 19,474 square feet of office and laboratory space in San Diego, California. The lease expires in May 2025. We believe that this facility is sufficient to meet our needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

We are not a party to any material legal proceedings at this time. From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our results of operations or financial condition. Regardless of the outcome, litigation can have an adverse effect on us because of defense and settlement costs, diversion of management resources and other factors.

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.

Market for Common Stock

Our common stock has been publicly traded on the Nasdaq Global Market under the symbol "TSBX" since our initial public offering on July 20, 2023.

Prior to that date, there was no public market for our common stock.

Holders of Common Stock

As of March 15, 2024, there were 23,099,335 shares of common stock issued and held by approximately 1,096 stockholders of record. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about securities authorized for issuance under our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

Issuer Purchases of Equity Securities

Not applicable.

Unregistered Sales of Equity Securities

Unregistered securities sold by us during the twelve months ended December 31, 2023 consisted of 279,707 shares of common stock issued upon the exercise of options and issuance of shares to Myst upon achievement of the first milestone for aggregate cash proceeds of $0.1 million.

The offers, sales and issuances of the securities described in the preceding paragraphs were deemed to be exempt from registration under the Securities Act in reliance on Section 4(a)(2) of the Securities Act or Rule 506 of Regulation D promulgated thereunder as a transaction by an issuer not involving a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof. Each of the recipients of securities in these transactions was either an accredited investor within the meaning of Rule 501 of Regulation D under the Securities Act or had adequate access, through employment, business or other relationships, to information about us. Appropriate legends were affixed to the securities issued in these transactions.

Use of Proceeds

On July 20, 2023, our Registration Statement on Form S-1 (File No. 333-272600) was declared effective by the SEC for our IPO. At the closing of the IPO on July 25, 2023, we sold 6,666,667 shares of common stock, at an

IPO price of $12.00 per share and received gross proceeds of $80.0 million, which resulted in net proceeds to us of approximately $68.7 million, after deducting underwriting discounts and commissions of $5.6 million and other offering costs totaling approximately $5.7 million. On August 15, 2023, the underwriters exercised their option to purchase an additional 651,608 shares of common stock at $12.00 per share. Aggregate net proceeds to the Company were $7.3 million after deducting underwriting discounts and commissions of $0.5 million. None of the expenses associated with the IPO were paid to directors, officers, persons owning ten percent or more of any class of equity securities, or to their associates, or to our affiliates, other than payments from our net proceeds in the ordinary course of business to officers for salaries and to non-employee directors as compensation for service on the board of directors or committees of the board of directors. BofA Securities, Inc., Leerink Partners LLC, and Piper Sandler & Co. acted as joint book-running managers for the IPO.

There has been no material change in the planned use of IPO proceeds from that described in the Final Prospectus.

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 financial statements and related notes and other financial information included in "Item 8. Financial Statements and Supplementary Data" in this Annual Report on Form 10-K. The following discussion contains forward-looking statements that involve risks and uncertainties. For a complete discussion of forward-looking statements, see the section above entitled "Special Note Regarding Forward Looking Statements." Our actual results could differ materially from those expressed or implied in any forward-looking statements as a result of various factors, including those set forth under the caption "Item 1A. Risk Factors."

Overview

We are a clinical stage biotechnology company focused on developing new medicines to treat and cure patients with solid tumors. Approved immunotherapies represent a significant advancement in the treatment of solid tumors, but many patients either do not respond or experience relapsed disease following an initial response. We believe the most significant challenge to creating curative immunotherapies in these patients is the low numbers of T cells that can recognize and attack the tumor, which we refer to as tumor-reactive T cells. To address this problem, we are pioneering a differentiated approach to tumor infiltrating lymphocytes, or TILs. We are developing next generation TIL therapies by selecting the most potent (meaning able to mediate an anti-tumor response) and tumor-reactive T cells, which we refer to as Selected TILs. Unlike other approaches that rely on standard "bulk TILs" that have demonstrated objective responses in clinical trials only in limited tumor types, we are developing our Selected TILs for potential treatment across the majority of solid tumors. We have three ongoing Phase 1 clinical trials for TIDAL-01, including a multi-site trial for the treatment of breast cancer, colorectal cancer, head and neck cancer, and uveal melanoma, and two investigator sponsored trials with H. Lee Moffitt Cancer Center and Research Institute, Inc., or Moffitt, across colorectal cancer, head and neck cancer, and both cutaneous and non-cutaneous melanomas. We intend to provide an initial clinical update across these two trials in mid-2024. We are also actively advancing our preclinical pipeline programs including TIDAL-02, our next Selected TIL program, and our TIDAL-01 viral immunotherapy combination program. We define objective response as a patient experiencing a partial response or complete response to any given therapy.

We are developing next generation TIL therapies for the potential treatment of multiple solid tumors. There are no TIL therapies that have received FDA approval to date. To our knowledge, at present there are no therapies in clinical development that provide curative outcomes for the majority of patients in our chosen solid tumor indications. Our innovative Selected TIL approach focuses on selecting and expanding the most potent tumor-reactive T cells to overcome the limitations of bulk TILs. This approach expands upon work conducted in academia that demonstrated improved clinical responses for certain selected TILs in solid-tumor types where bulk TILs have not shown objective responses in clinical trials. We are leveraging this work to establish a standardized manufacturing process for large scale production of our Selected TILs.

We are applying our Selected TIL approach for potential treatment of a wide range of solid tumors. We are developing a broad pipeline aimed at improving outcomes for patients, as illustrated in the chart below.

Programs		Product Overview	Key Indications	Preclinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestone
Selected TILs	TIDAL-01	Tumor-reactive Selected TILs	Breast cancer; CRC; HNSCC; Uveal melanoma					Initial clinical data in mid-2024
			CRC; Cutaneous and non-cutaneous melanomas; HNSCC		Moffitt Collaboration*			
		Combination with viral immunotherapy	Solid tumors					IND submission
	TIDAL-02	Selected TILs with next-gen manufacturing and TIL quality enhancements	Solid tumors					IND submission

* Two concurrent investigator sponsored trials at Moffitt Cancer Center

CRC - Colorectal cancer; HNSCC - Head and neck squamous cell carcinoma

We are advancing TIDAL-01, our lead Selected TIL product candidate, for the treatment of multiple solid tumor indications. TIDAL-01 utilizes an unbiased identification and functional screening process to isolate and selectively expand the greatest breadth of tumor-reactive TILs from the patient's tumor. Our TIDAL-01 production process is designed to deliver at least 10^9 cells and targets greater than 70% functional and potent tumor-reactive T cells.

We have three ongoing Phase 1 clinical trials for TIDAL-01, including a multi-site trial for the treatment of breast cancer, colorectal cancer, head and neck cancer, and uveal melanoma, and two investigator sponsored trials with Moffitt across colorectal cancer, head and neck cancer, and both cutaneous and non-cutaneous melanomas. Our next Selected TIL program, TIDAL-02, is being designed to encompass a next generation streamlined manufacturing process for tumor-reactive T cells and additional modifications to enhance TIL quality and function. We believe that TIDAL-02 has the potential to address the medical need in solid tumor indications that are distinct from and complementary to TIDAL-01. TIDAL-02 is currently in preclinical development. We intend to evaluate the combination of TIDAL-01 with viral immunotherapy through two approaches: (1) treatment of the patient with viral immunotherapy prior to TIL extraction to optimize TIL harvest and broaden applicability to additional tumor types with low immune cell infiltration and (2) treatment of the patient with viral immunotherapy following treatment with TIDAL-01 to optimize TIL trafficking and infiltration into solid tumors and to support the anti-tumor functions of infiltrating immune cells. We are currently evaluating the optimal viral immunotherapy for combination with TIDAL-01 to advance into clinical development.

Our headquarters are located in San Diego, California and we operate as one segment. Since our inception, we have devoted substantially all of our efforts and financial resources to organizing and staffing our company, business planning, raising capital, discovering product candidates and securing related intellectual property rights and conducting research and development activities for our Selected TIL programs and product candidates. We do not have any products approved for sale and we have not generated any revenue from product sales and have incurred overall net losses since our inception through December 31, 2023. We have funded our operations primarily through the sale of our convertible preferred stock and revenue from certain of our collaboration agreements as well as our recent IPO. Since our inception, we have raised an aggregate of approximately $172.0 million of gross proceeds from the issuance and sale of shares of our convertible preferred stock, $190.0 million in upfront, non-refundable collaboration revenue, and most recently, raised $80.0 million with gross proceeds from the IPO completed on July 25, 2023 and $7.8 million from the exercise of the underwriters option to purchase additional shares. As of December 31, 2022 and December 31, 2023, we had cash, cash equivalents and short-term investments of $82.1 million and $94.8 million, respectively.

We have incurred significant operating losses in the past, and we expect to continue to incur significant operating losses for the foreseeable future. We incurred a net loss of $30.8 million and $55.2 million for the twelve months ended December 31, 2022 and 2023, respectively. As of December 31, 2022 and December 31, 2023, we had an accumulated deficit of $121.6 million and $176.8 million, respectively. Substantially all of our operating losses result from expenses incurred in our research and development programs and from general and administrative costs associated with our operations. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current or future product candidates, and on our ability to enter into collaborations, strategic partnerships and alliances or marketing, distribution or licensing arrangements with third parties.

We expect to incur significant expenses and increasing operating losses for the foreseeable future as we continue the preclinical development, manufacturing and clinical development of, and seek regulatory approval for, our product candidates. In addition, we may incur expenses in connection with the in-license or acquisition of additional platform technologies and the development of any such product candidates. We also expect to incur additional costs associated with operating as a public company. Furthermore, our operating losses may fluctuate significantly from quarter to quarter and year to year due to timing of preclinical activities, clinical development and regulatory approval of our product candidates.

We plan to fund future operations and future capital funding needs through equity and debt financings, licensing transactions, and collaborations or strategic partnerships with other companies. We can provide no assurance that financing will be available in the amounts we need or on terms acceptable to us, if at all. If we enter into licensing transactions, collaborations, strategic partnerships or similar agreements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and may reduce the value of our common stock. If we are not able to secure adequate additional funding, we may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, and suspend, delay or curtail our development programs. Any of these actions could materially harm our business.

Our innovative Selected TIL approach focuses on selecting and manufacturing the most potent tumor reactive T cells to overcome the limitations of bulk TILs. This approach is grounded on work conducted in academia that has demonstrated improved clinical responses for selected TILs in solid tumor types where bulk TILs have not shown benefit. We are leveraging this work to establish a standardized manufacturing process for large scale production of our Selected TILs. We intend to establish in-house tumor sequencing capabilities, expedite manufacturing and shipping of peptides, and biopsy tumor prior to resection to enable earlier sequencing and peptide synthesis.

Macroeconomic and Geopolitical Trends

We continue to actively monitor the impact of various macroeconomic and geopolitical trends, such as high rates of inflation, supply chain disruptions and geopolitical instability, and bank failures on our business. To date, we have not experienced a material financial statement impact or business disruptions, including with our vendors or third parties, as a result of these negative macroeconomic or geopolitical trends. Our business has been, and may continue to be, impacted by the negative macroeconomic and geopolitical trends wherever we have clinical trial sites, contract manufacturing organizations, or CMOs, facilities or other business operations.

Global economic and business activities continue to face widespread uncertainties, and global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, rising inflation and monetary supply shifts, rising interest rates, labor shortages, declines in consumer confidence, declines in economic growth, increases in unemployment rates, recession risks, and uncertainty about economic and geopolitical stability. Moreover, negative macroeconomic conditions could adversely impact our ability to obtain financing in the future on terms acceptable to us, or at all. In

addition, the geopolitical instability and related sanctions could continue to have significant ramifications on global financial markets, including volatility in the U.S. and global financial markets.

Reverse Stock Split

On July 14, 2023, we effected a 1-for-7.9872 reverse stock split, or Reverse Split, of our issued and outstanding shares of common stock and a proportional adjustment to the conversion ratio for each of our outstanding series of redeemable convertible preferred stock. All share and per share amounts have been retroactively adjusted, where applicable, to reflect the Reverse Split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital. Shares of common stock underlying outstanding stock options and restricted stock were proportionately reduced and the respective exercise prices, if applicable, were proportionately increased in accordance with the terms of the appropriate securities agreements. Stockholders entitled to fractional shares as a result of the Reverse Split received a cash payment in lieu of receiving fractional shares.

Initial Public Offering

On July 25, 2023, we completed our IPO pursuant to which we issued and sold an aggregate of 6,666,667 shares of common stock at a price to the public of $12.00 per share. Aggregate net proceeds to us were $68.7 million after deducting underwriting discounts and commissions of $5.6 million and other offering expenses of $5.7 million. On August 15, 2023, the underwriters exercised their option to purchase an additional 651,608 shares of common stock at $12.00 per share. Aggregate net proceeds to us was $7.3 million after deducting underwriting discounts and commissions of $0.5 million. Upon the closing of the IPO, all outstanding shares of redeemable convertible preferred stock automatically converted into shares of common stock. Subsequent to the closing of the IPO, there were no shares of redeemable convertible preferred stock outstanding.

In connection with the closing of the IPO, we filed our Amended and Restated Certificate of Incorporation which provides that the authorized capital stock is 500,000,000 shares consisting of 490,000,000 shares of common stock and 10,000,000 shares of undesignated preferred stock, both with a par value of $0.001 per share.

Collaboration Agreements

Below is a summary of the key terms for certain of our collaboration agreements. For a more detailed description of our collaboration agreements, see Note 6 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Moffitt Collaboration Agreements

Master Collaboration Agreement

In January 2021, we entered into an amended and restated master collaboration agreement, or the Moffitt Agreement, with Moffitt, to amend a then-existing master collaboration agreement from November 2019, as amended March 2020, between Moffitt and our now wholly-owned subsidiary, Myst Therapeutics LLC, with the intent to continue to work collaboratively in the research of cancer immunotherapies.

Moffitt granted us (1) a royalty-free, sublicensable, non-transferable, perpetual, non-exclusive license to use and practice certain inventions invented solely by Moffitt in the performance of a research plan or through use of any data generated thereunder, or Moffitt Inventions, (a) for internal, non-commercial research purposes outside the field of adoptive cell therapy and/or (b) to research, develop, make, use, sell, offer to sell, or import products and/or services in the field of adoptive cell therapy and (2) a royalty free, sublicensable, non-transferable, perpetual, non-exclusive license to use and practice certain inventions invented in performance of a research plan or through the use of Moffitt research materials, which are (i) specifically directed to the identity of melanoma-specific T cell receptors, (ii) invented during the collaboration term or within one year after the end of the collaboration term within the field of adoptive cell therapy, and (iii) invented solely by either parties' employees or by both parties' employees

jointly, to research, develop, make, use, sell, offer to sell, or import products and/or services for cancer immunotherapy involving identifying relevant tumor reactive T cells from TILs.

Moffitt Alliance Agreement

In June 2022, we entered into a life science alliance agreement with Moffitt, or the Alliance Agreement, in order to further expand our relationship and support our existing agreements with Moffitt, or the Underlying Agreements. Pursuant to the Alliance Agreement, we will have priority access to Moffitt's scientific research, manufacturing, and clinical capabilities for the development of novel TIL therapies, including expedited clinical trial activation, enhanced patient screening and data sharing, access to Moffitt's cellular therapies research and development infrastructure, expanded molecular data sets and biospecimens for research, and allocated cGMP manufacturing capacity for our product candidates.

Under the Alliance Agreement, we are obligated to use commercially reasonable efforts to further develop TIL Products (as defined below), to manufacture TIL Products, to obtain regulatory approval for at least one TIL Product in the United States and to commercialize TIL Products in all countries in which regulatory approval for a TIL Product has been obtained. For purposes of the Alliance Agreement, TIL Product means any pharmaceutical, biopharmaceutical, or biotechnology TIL product that has been developed by us or Moffitt and is advanced into clinical development under an IND sponsored by Moffitt.

Pursuant to the Alliance Agreement, we agreed to pay to Moffitt a total amount of at least $17.5 million, or Alliance Funding Amount, for research, development and manufacturing related services that will be paid equally over five years on June 1st of each year starting on June 1, 2023. The Alliance Funding Amount will be calculated annually at the conclusion of each payment period, and, to the extent our annual aggregate payments to Moffitt of $3.5 million exceeds the applicable annual installment amount, we will receive a reduction in the amount due for future installment payments based on a predetermined formula agreed to by the parties. To the extent the aggregate annual payments are less than $3.5 million, we will prepay the remaining amount due.

In connection with the execution of the Alliance Agreement, we issued Moffitt 91,721 shares of our common stock. As partial consideration under the Alliance Agreement, we also agreed to issue Moffitt an additional 366,884 shares of our common stock in the aggregate upon the satisfaction of certain clinical and regulatory milestones with respect to TIL Products. During the twelve months ended December 31, 2023, an additional 91,721 shares of our common stock were issued to Moffitt as a result of the achievement of the milestone related to the start of the Phase 1 clinical trial for a TIL Product. In addition, upon achievement of certain thresholds for aggregate net sales of all TIL Products, we are required to make tiered sales-based milestones payments to Moffitt of up to an aggregate of $50.0 million. With respect to each of the equity and sales milestones described above, TIL Products include any pharmaceutical, biopharmaceutical or biotechnology TIL product that is developed by us or Moffitt and is advanced into clinical development under an IND sponsored by Moffitt.

Components of Our Results of Operations

Revenue

Collaboration Revenue

We enter into collaboration arrangements that may include the receipt of payments for up-front fees, success-based milestones, option exercises, intellectual property rights, research services, product supplies, and royalties on any future sales of commercialized products that result from the collaborations.

Takeda Pharmaceutical Company Limited

In November 2019, we entered into a discovery, collaboration and license agreement, or the Takeda Agreement, with Millennium Pharmaceuticals, Inc. (also known as Takeda Oncology), a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited, or Takeda. Under the Takeda Agreement, Takeda paid us an upfront payment of $50.0 million and an additional upfront payment of $30.0 million for the option to license up to two

selected discovery candidates, with additional consideration in the low to low-mid eight figures to be paid to us by Takeda for each exercise of such option.

The Takeda Agreement accounted for 100% of our total collaboration revenue for the twelve months ended December 31, 2023 and 2022.

On June 13, 2022, Takeda provided us with six months' written notice to terminate the development program in accordance with its termination for convenience rights, with such termination being effective as of December 13, 2022. Upon the effective termination date of December 13, 2022, Takeda's co-exclusive license to TBio-6517 terminated and we are no longer obligated to pursue development of TBio-6517. On January 6, 2023, Takeda provided us with six months' written notice to terminate the remainder of the Takeda Agreement, in accordance with its termination for convenience rights, with such termination being effective as of July 6, 2023. As of March 31, 2023, we ceased all work under the Takeda Agreement and we have concluded that there are no remaining estimated services associated with the obligations under the Takeda Agreement as of the effective date of termination of the Takeda Agreement in its entirety. We will not receive any additional collaboration revenue under the Takeda Agreement in the future because this agreement has been terminated.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of external and internal costs incurred for our research and development activities, including adjusted development of our platform, our product discovery efforts and the development of our future product candidates. We expense research and development costs as incurred.

External costs include:

- clinical trial expenses, including costs of third-party CROs and costs of performing toxicity studies;
- expenses to acquire technologies to be used in research and development;
- manufacturing scale-up expenses and the cost of acquiring and manufacturing preclinical and clinical materials and developing manufacturing processes; and
- costs related to compliance with regulatory requirements.

Internal costs include:

- employee-related expenses, which include salaries, benefits and stock-based compensation for employees engaged in research and development functions; and
- facility-related and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation and amortization expense and expenses related to other general support services and supplies.

Costs for external development activities are recognized based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our consolidated financial statements as prepaid or accrued research and development expenses. Non-refundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses and expensed as the related goods are delivered or the services are performed.

The table below summarizes our research and development expenses incurred by major development program for the periods presented *(in thousands)*:

	Year Ended December 31,	
	2023	2022
RIVAL-01	$ 845	$ 32,078
TIDAL-01	46,960	36,542
TIDAL-02	6,154	5,893
Other research programs	6,532	12,190
Total research and development	$ 60,491	$ 86,703

The successful development of our product candidates is highly uncertain. We plan to substantially increase our research and development expenses for the foreseeable future as we continue our existing clinical trials, initiate future clinical trials for our product candidates, continue to discover and develop additional product candidates, improve the efficiency and scalability of our manufacturing processes and supply chain and build our in-house process development, analytical and manufacturing capabilities. Therefore, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development and commercialization of any of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from the sale of our current or any future product candidates, if approved. This is due to the numerous risks and uncertainties associated with developing product candidates, including the uncertainty of:

- the scope, rate of progress and expenses of our planned clinical trials and other research and development activities;
- successful patient enrollment in, and the initiation and completion of, clinical trials including the impact of patient discontinuations and the number and location of clinical sites;
- establishing an appropriate safety profile of our product candidates;
- whether our product candidates show safety and efficacy in our clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- making arrangements with third-party manufacturers for the supply of materials to support our planned clinical trials and establishing commercial manufacturing capabilities for the potential manufacture of approved products, if any;
- obtaining, maintaining, protecting and enforcing patent and trade secret protection and regulatory exclusivity for our product candidates;
- commercializing product candidates, if and when approved, whether alone or in collaboration with others; and
- acceptable safety profile of the products following any regulatory approval.

Any changes in the outcome of any of these variables with respect to the development of our product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. For example, if the FDA or comparable foreign regulatory authority were to delay our planned clinical trials or require us to conduct pre-clinical or clinical trials beyond those that we currently expect or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel costs, allocated expenses and other expenses for outside professional services, including legal, intellectual property, human resources, audit and accounting services. Personnel costs consist of salaries, bonuses, benefits and stock-based compensation.

We expect our general and administrative expenses will increase during the next few years to support our continued research and development activities of our product candidates and associated expenses with operating as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, or SEC and Nasdaq, insurance expenses, audit expenses, investor relations activities, Sarbanes-Oxley Act compliance expenses, increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other administrative expenses and professional services.

Other Income, Net

Other income, net consists primarily of interest income earned on our short-term investments and foreign currency remeasurement gains and losses.

Results of Operations

Comparison of the Years Ended December 31, 2023 and 2022

The following tables set forth our results of operations (*in thousands*):

	Year Ended December 31,		
	2023	2022	Change ($)
Collaboration revenue	$ 19,306	$ 73,300	$ (53,994)
Operating expenses:			
Research and development	60,491	86,703	(26,212)
General and administrative	17,847	18,223	(376)
Total operating expenses	78,338	104,926	(26,588)
Loss from operations	(59,032)	(31,626)	(27,406)
Other income, net	3,546	933	2,613
Benefit (provision) for income taxes	286	(141)	427
Net loss	$ (55,200)	$ (30,834)	$ (24,366)

Collaboration Revenue

Collaboration revenue was $19.3 million and $73.3 million during the twelve months ended December 31, 2023 and 2022, respectively, a decrease of $54.0 million, or 73.7%. The change was due to recognition of deferred revenue as a result of the termination of the Takeda Agreement resulting in all remaining deferred revenue recognized by the first quarter of fiscal year 2023.

Research and Development Expenses

The following table summarizes our research and development expenses *(in thousands)*.

	Year Ended December 31,	
	2023	2022
Pre-clinical research and development	$ 10,267	$ 19,530
Manufacturing	24,089	42,221
Clinical and regulatory	6,870	6,521
Personnel related	19,265	18,431
Total research and development	$ 60,491	$ 86,703

Research and development expenses were $60.5 million and $86.7 million during the years ended December 31, 2023 and 2022, respectively, a decrease of $26.2 million, or 30.2%. The decrease was due primarily to a decrease of $9.2 million in pre-clinical research costs and $18.1 million in manufacturing expenses due to the termination of the Takeda agreement and winding down activities related to the RIVAL-01 platform offset by increases of $0.9 million in personnel-related costs, and $0.4 million in clinical and regulatory costs. Due to the termination of the Takeda Agreement and research and development activities thereunder, we expected our research and development expenses to decline during the twelve months ended in December 2023 as compared to the twelve

months ended in December 2022; however, we expect our research and development expenses to increase over the long term as we advance the development of our product candidates.

General and Administrative Expenses

General and administrative expenses were $17.9 million and $18.2 million during the years ended December 31, 2023 and 2022, respectively, a decrease of $0.4 million, or 2.2%. We anticipate that general and administrative expenses will remain stable as we support public company operations.

Other Income (Expense), Net

Other income (expense), net was $3.5 million and $0.9 million during the years ended December 31, 2023 and 2022, respectively, an increase of $2.6 million, or 288.9%. The increase was primarily due to interest income earned on the net proceeds from our recently completed IPO and the Federal Reserve increasing interest rates.

Liquidity and Capital Resources

In December 2018, we completed a corporate reorganization pursuant to which Turnstone Biologics Inc. merged with and into Turnstone Biologics Corp., a newly formed Delaware corporation, as the successor company. As a result of this reorganization, we changed our domicile from the country of Canada to the State of Delaware. Our headquarters are located in San Diego, California and we operate as one segment. Since our inception, we have devoted substantially all of our efforts and financial resources to organizing and staffing our company, business planning, raising capital, discovering product candidates and securing related intellectual property rights and conducting research and development activities for our Selected TIL programs and product candidates. We do not have any products approved for sale, we have not generated any revenue from product sales, and we have incurred overall net losses since our inception through December 31, 2023.

We have evaluated and concluded there are no conditions or events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern for a period of one year following the date these consolidated financial statements are issued and believe our existing cash and cash equivalents and short-term investments as of December 31, 2023 of $94.8 million will be sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2025.

Prior to our IPO and since our inception, we have funded our operations primarily through the sale of our convertible preferred stock and revenue from certain of our collaboration agreements. Since our inception, we have raised an aggregate of approximately $172.0 million of gross proceeds from the issuance and sale of shares of our convertible preferred stock, $190.0 million in upfront, nonrefundable collaboration revenue, and most recently, with gross proceeds of $80.0 million from the IPO completed on July 25, 2023 and $7.8 million from the exercise of the underwriters' option to purchase additional shares. As of December 31, 2022 and December 31, 2023, we had cash, cash equivalents and short-term investments of $82.1 million and $94.8 million, respectively.

We have incurred significant operating losses in the past and expect to continue to incur significant operating losses for the foreseeable future. Our net loss was $30.8 million and $55.2 million for the twelve months ended December 31, 2022 and 2023, respectively. As of December 31, 2022 and December 31, 2023, we had an accumulated deficit of $121.6 million and $176.8 million, respectively. Substantially all of our operating losses result from expenses incurred in our research and development programs and from general and administrative costs associated with our operations. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current or future product candidates, and on our ability to enter into collaborations, strategic partnerships and alliances or marketing, distribution or licensing arrangements with third parties.

We expect that our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2025. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we continue to advance our product candidates and programs through preclinical and clinical development. Furthermore, as a result of the completion of the IPO on July 25, 2023, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs which could materially harm our business.

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

- the costs of conducting clinical trials, including the clinical development of our TIDAL-01 product candidate;
- the progress of preclinical development and clinical trials of our current earlier-stage and future product candidates;
- the costs of manufacturing;
- the scope, progress, results and costs of discovery, preclinical development, laboratory testing and clinical trials for other potential product candidates we may develop, if any;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaborations and partnerships on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any collaboration agreements we might have at such time;
- the costs of preparing, filing and prosecuting patent applications, obtaining, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the cost of operating as a public company;
- the costs and timing of future commercialization activities, if any, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- our ability to achieve sufficient market acceptance, adequate coverage and reimbursement from third-party payors and adequate market share; and
- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

As of December 31, 2022 and December 31, 2023, we had cash, cash equivalents and short-term investments of $82.1 million and $94.8 million, respectively. We believe that our existing cash, cash equivalents and short-term investments, will enable us to fund our operating expenses and capital expenditures into the second quarter of 2025. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. We anticipate that we will require additional capital as we seek regulatory approval of our product candidates and if we choose to pursue in-licenses or acquisitions of other product candidates. If we need to raise additional capital to fund our operations, funding may not be available to us on acceptable terms, or at all. If we are unable to obtain adequate financing when needed, we may have to delay, reduce

the scope of, or suspend one or more of our preclinical studies, clinical trials, research and development programs, or commercialization efforts. If we receive regulatory approval for our current or future product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interests may be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may need to significantly delay, scale back or discontinue the development or future commercialization of one or more of our product candidates, if approved, or one or more of our other research and development initiatives and we may need to undertake additional workforce reductions or restructuring activities in the future. Any of the above events could adversely affect our business, results of operations and financial condition and cause the price of our common stock to decline.

Cash Flows

The following table summarizes our cash flows *(in thousands)*:

	Year Ended December 31,	
	2023	2022
Cash used in operating activities	$ (66,152)	$ (71,062)
Cash used in investing activities	(28,093)	(14,932)
Cash provided by (used in) financing activities	77,046	(2,656)
Net decrease in cash, cash equivalents and restricted cash	$ (17,199)	$ (88,650)

Cash Flows from Operating Activities

Net cash used in operating activities for the year ended December 31, 2023 was $66.2 million, primarily due to our net loss of $55.2 million and the decrease in our net operating assets and liabilities of $17.9 million, which included changes in deferred revenue of $19.3 million, accretion of the premium on short-term investments of $2.1 million and partially offset by changes in stock-based compensation of $4.2 million, depreciation and amortization expense of $2.8 million, impairment of long-lived assets of $1.6 million, and loss on disposal of property and equipment of $0.3 million.

Net cash used in operating activities for the year ended December 31, 2022 was $71.1 million, primarily due to our net loss of $30.8 million and decrease in our net operating assets and liabilities of $58.0 million, which included changes in deferred revenue of $53.1 million, partially offset by changes in stock-based compensation and Moffitt performance awards of $6.4 million, depreciation and amortization expense of $3.9 million, impairment of ROU asset of $0.5 million and change in the fair value of contingent consideration liabilities of $7.0 million.

Cash Flows from Investing Activities

Net cash used in investing activities for the year ended December 31, 2023 was $28.1 million, due primarily to $109.8 million in purchases of short-term investments and $1.3 million in purchases of property and equipment

offset by the maturities of $82.5 million of short-term investments and $0.5 million of proceeds from the sale of property and equipment.

Net cash used in investing activities for the year ended December 31, 2022 was $14.9 million, due primarily to the purchase of short-term investments of $59.5 million and $5.2 million in purchases of property and equipment offset by the maturities of short-term investments of $49.8 million.

Cash Flows from Financing Activities

Net cash provided by financing activities for the year ended December 31, 2023 was $77.0 million, due primarily to $77.8 in proceeds from our IPO, net of issuance costs and $0.1 million from the exercise of stock options offset by $0.9 million cash payment of contingent consideration related to Myst's achievement of the first and second milestone under the Myst Merger Agreement.

Net cash used in financing activities for the year ended December 31, 2022 was $2.7 million, due primarily to the $2.8 million cash payment of contingent consideration related to Myst's achievement of the second milestone offset by $0.2 million from the exercise of stock options.

Contractual Obligations and Commitments

We enter into contracts in the normal course of business with CROs and CMOs for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts provide for termination at the request of either party with less than one year notice, and therefore we believe that our non-cancellable obligations under these agreements are not material. We additionally have contractual obligations for our operating leases for our corporate headquarters and office and laboratory spaces. These obligations are further described in Note 11 to our consolidated financial statements. We are also party to certain collaboration and license agreements, which contain a number of contractual obligations. Those contractual obligations may entitle us to receive, or may obligate us to make, certain payments. The amount and timing of those payments are unknown or uncertain as we are unable to estimate the timing or likelihood of the events that will obligate those payments.

We have milestones, royalties, and/or other payments due to third parties under our existing license and collaboration agreements. See Note 6 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K. We can't estimate when such payments will be due and none of these events were probable to occur as of December 31, 2022 and December 31, 2023, respectively.

Critical Accounting Polices and Estimates

The preparation of our financial statements and related disclosures in conformity with generally accepted accounting principles in the United States and our discussion and analysis of our financial condition and operating results require us to make judgments, assumptions and estimates that affect the amounts reported in our consolidated financial statements and accompanying notes. Our significant accounting policies and methods used in preparation of our consolidated financial statements are described in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. We base our estimates on historical experience and on various other assumptions we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results may differ from these estimates, and such differences may be material.

Accrued Research and Development Expenses

Research and development costs are expensed as incurred. Research and development costs consist of payroll and other personnel-related expenses, materials and supplies, preclinical expenses, manufacturing expenses, contract research and development services, and consulting costs, as well as allocations of facilities and other overhead costs. Costs of certain development activities, such as manufacturing, are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development costs. Non-refundable advance payments for goods or

services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. Costs associated with collaboration agreements are included in research and development expenses. Assets acquired that are used for research and development and which have no alternative use are expensed to research and development costs.

We makes estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on the facts and circumstances known at that time. Accrued expenses for preclinical studies and clinical trials are based on estimates of costs incurred and fees that may be associated with services provided by contract research organizations ("CROs"), clinical trial investigational sites and other clinical trial-related activities. Payments under certain contracts with such parties depend on factors such as successful enrollment of patients, site initiation and the completion of clinical trial milestones. In accruing for these services, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If possible, we obtain information regarding unbilled services directly from these service providers. However, we may be required to estimate these services based on other available information. If we underestimate or overestimate the activities or fees associated with a study or service at a given point in time, adjustments to research and development expenses may be necessary in future periods. Historically, estimated accrued liabilities have approximated actual expenses incurred. Subsequent changes in estimates may result in a material change in accruals.

Stock-Based Compensation

We account for stock-based compensation expense related to stock options and restricted stock units or RSUs, by estimating the fair value on the date of grant. We estimate the fair value of stock options granted to employees and non-employees using the Black-Scholes option pricing model. The fair value of RSUs granted to employees is the closing price of our common stock on the date of grant. We recognize stock-based compensation expense, over the requisite service period, based on the vesting provisions of the individual grants. Generally, we issue stock-based awards with only service-based vesting conditions and records the expense for these awards using the straight-line method. We account for forfeitures when they occur.

The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (a) the expected stock price volatility, (b) the expected term of the award, (c) the risk-free interest rate and (d) expected dividend yields. Due to the lack of a public market for our common stock until July 20, 2023, and lack of company-specific historical and implied volatility data, we have based our computation of expected volatility on the average historical volatility of a representative group of public companies with similar characteristics to us, including stage of product development and life science industry focus. The historical volatility is calculated based on a period of time commensurate with the expected term. We use the simplified method as prescribed by the U.S. Securities and Exchange Commission Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as we do not expect substantially different exercise or post-vesting termination behavior among our employee population. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as we have never paid dividends and have no current plans to pay any dividends on its common stock.

Impairment of Long-Lived Assets

We review long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable, including evaluating the impact of the overall micro- and macro-economic conditions on the carrying value of our long-lived assets, including property and equipment and operating lease assets. During the year ended December 31, 2023, our stock price and resulting market capitalization experienced a significant, sustained decline. Accordingly, we assessed our long-lived assets, including property and equipment and operating lease assets for impairment. Recoverability of these assets is determined by comparing the forecasted undiscounted net cash flows of the operation to which the assets relate to the carrying amount. If the operation is determined to be unable to recover the carrying amount of its assets, then these assets are written down first to fair value Fair value is determined based on discounted cash flows or appraised values, depending on the nature of the assets.

We recognized long-lived asset impairment charges of $1.6 million and $0.5 million for the years ended December 31, 2023 and 2022, respectively.

Contingent Consideration

Consideration paid related to the Myst Merger Agreement may include potential future payments that are contingent upon our achieving certain milestones in the future. Contingent consideration liabilities are measured at their estimated fair value as of the date of the consolidated balance sheets using a probability-based income approach based on the monetary value of the milestone payment discounted for the likelihood of achieving the milestone and a present value factor based on the timing of when the milestone is expected to be achieved. Contingent consideration liabilities expected to be settled within 12 months after the balance sheet date are presented in current liabilities, with the non-current portion recorded under other liabilities, non-current in the consolidated balance sheets. Changes in the fair value of the contingent consideration are recorded as research and development expenses in the consolidated statement of operations and comprehensive loss.

Accounting Pronouncements Recently Adopted

See Note 2 to our audited consolidated financial statements included elsewhere in this Annual Report for a description of recent accounting pronouncements applicable to our financial statements.

Emerging Growth and Smaller Reporting Company Status

The JOBS Act permits an "emerging growth company" such as us to take advantage of reduced reporting requirements that are otherwise applicable to public companies and also an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to not "opt out" of this provision and, as a result, we will adopt new or revised accounting standards at the time private companies adopt the new or revised accounting standard and will do so until such time that we either (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an emerging growth company.

We will remain an emerging growth company until the earliest of (i) December 31, 2027, (ii) the last day of the fiscal year in which we have total annual gross revenues of $1.235 billion or more, (iii) the date on which we have issued more than $1.0 billion in non-convertible debt during the previous rolling three-year period or (iv) the date on which we are deemed to be a large accelerated filer under the Exchange Act.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our ordinary shares held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than $100.0 million during the most recently completed fiscal year and our ordinary shares held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are a smaller reporting company, as defined in Rule 12b-2 under the Exchange Act, for this reporting period and are not required to provide the information required under this item

Item 8. Financial Statements and Supplementary Data

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Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Turnstone Biologics Corp.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Turnstone Biologics Corp. (the Company) as of December 31, 2023 and 2022, the related consolidated statements of operations and comprehensive loss**,** redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2023, 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, 2023 and 2022, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2023 in conformity with U.S. generally accepted accounting principles.

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 Public Company Accounting Oversight Board (United States) (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. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018.

San Diego, California
March 21, 2024

Turnstone Biologics Corp.
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	December 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 17,798	$ 34,731
Restricted cash	116	382
Short-term investments	76,979	47,330
Accounts receivable - collaboration agreement	194	8,728
Prepaid expenses	4,655	5,081
Other current assets	2,812	1,749
Total current assets	102,554	98,001
Other assets, noncurrent	1,143	2,582
Operating lease right of use assets	2,766	4,631
Property and equipment, net	6,352	9,724
Total assets	$ 112,815	$ 114,938
Liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 36	$ 3,435
Accrued expenses and other current liabilities	9,909	14,287
Operating lease liability, current	2,025	1,961
Deferred revenue, current	—	15,144
Total current liabilities	11,970	34,827
Deferred revenue, noncurrent	—	4,162
Operating lease liability, noncurrent	1,189	3,205
Other liabilities, noncurrent	989	2,267
Total liabilities	14,148	44,461
Redeemable convertible preferred stock		
Series A redeemable convertible preferred stock, $0.001 par value; authorized, issued and outstanding shares - 0 and 11,250,000 at December 31, 2023 and 2022, respectively; liquidation preference - $0 and $8,643 at December 31, 2023 and 2022, respectively	—	8,643
Series B-1 redeemable convertible preferred stock $0.001 par value; authorized, issued and outstanding shares - 0 and 16,285,156 at December 31, 2023 and 2022, respectively; liquidation preference - $0 and $12,611 at December 31, 2023 and 2022, respectively	—	12,611
Series B-2 redeemable convertible preferred stock $0.001 par value; authorized, issued and outstanding shares - 0 and 25,065,538 at December 31, 2023 and 2022, respectively; liquidation preference - $0 and $28,860 at December 31, 2023 and 2022, respectively	—	28,860
Series C redeemable convertible preferred stock $0.001 par value; authorized, issued and outstanding shares - 0 and 17,905,288 at December 31, 2023 and 2022, respectively; liquidation preference - $0 and $42,100 at December 31, 2023 and 2022, respectively	—	42,100
Series D redeemable convertible preferred stock $0.001 par value; authorized, issued and outstanding shares - 0 and 29,285,356 at December 31, 2023 and 2022, respectively; liquidation preference - $0 and $80,000 at December 31, 2023 and 2022, respectively	—	79,730
Total redeemable convertible preferred stock	—	171,944
Stockholders' equity (deficit)		
Preferred stock, $0.001 par value; 10,000,000 and 0 shares authorized at December 31, 2023 and 2022, respectively, 0 shares issued and outstanding at December 31, 2023 and 2022, respectively	—	—
Common stock, $0.001 par value; 490,000,000 and 147,892,358 shares authorized, 23,099,335 and 2,915,757 shares issued and outstanding as of December 31, 2023 and 2022, respectively	23	3
Additional paid-in capital	275,521	20,501
Accumulated other comprehensive loss	(119)	(413)
Accumulated deficit	(176,758)	(121,558)
Total stockholders' equity (deficit)	98,667	(101,467)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 112,815	$ 114,938

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

Turnstone Biologics Corp.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,	
	2023	2022
Collaboration revenue	$ 19,306	$ 73,300
Operating expenses:		
Research and development	60,491	86,703
General and administrative	17,847	18,223
Total operating expenses	78,338	104,926
Loss from operations	(59,032)	(31,626)
Other income, net	3,546	933
Net loss before income taxes	(55,486)	(30,693)
Benefit (provision) for income taxes	286	(141)
Net loss	$ (55,200)	$ (30,834)
Other comprehensive income (loss):		
Unrealized gain (loss) on available-for-sale debt securities	294	(168)
Total comprehensive loss	$ (54,906)	$ (31,002)
Net loss	$ (55,200)	$ (30,834)
Less: accretion of preferred stock to redemption value	$ (39)	$ (190)
Net loss attributable to common stockholders, basic and diluted	$ (55,239)	$ (31,024)
Weighted-average shares of common stock outstanding, basic and diluted	11,562,910	2,484,569
Net loss per share attributable to common stockholders, basic and diluted	$ (4.78)	$ (12.49)

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

Turnstone Biologics Corp.
Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share amounts)

	Series A Redeemable Convertible Preferred Stock		Series B-1 Redeemable Convertible Preferred Stock		Series B-2 Redeemable Convertible Preferred Stock		Series C Redeemable Convertible Preferred Stock		Series D Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2021	11,250,000	$ 8,582	16,285,156	$ 12,611	25,065,538	$ 28,860	17,905,288	$ 42,048	29,285,356	$ 79,653	2,550,478	$ 3	$ 9,115	$ (245)	$ (90,724)	$ (81,851)
Accretion of redeemable convertible preferred stock issuance costs		$ 61						$ 52		$ 77			$ (190)			$ (190)
Issuance of common stock upon Myst milestone achievement											212,203		$ 5,000			$ 5,000
Moffitt performance based common stock award											91,721		$ 2,051			$ 2,051
Exercise of stock options											61,355		$ 157			$ 157
Stock-based compensation expense													$ 4,368			$ 4,368
Unrealized loss on available-for-sale debt securities														$ (168)		$ (168)
Net Loss															$ (30,834)	$ (30,834)
Balance at December 31, 2022	11,250,000	$ 8,643	16,285,156	$ 12,611	25,065,538	$ 28,860	17,905,288	$ 42,100	29,285,356	$ 79,730	2,915,757	$ 3	$ 20,501	$ (413)	$ (121,558)	$ (101,467)
Proceeds from IPO, net of issuance costs											7,318,275	$ 7	$ 75,956			$ 75,963
Accretion of redeemable convertible preferred stock issuance costs										$ 39			$ (39)			$ (39)
Conversion of redeemable convertible preferred stock to common stock due to the IPO	(11,250,000)	$ (8,643)	(16,285,156)	$ (12,611)	(25,065,538)	$ (28,860)	(17,905,288)	$ (42,100)	(29,285,356)	$ (79,769)	12,493,879	$ 13	$ 171,970			$ 171,983
Issuance of common stock upon Myst milestone achievement											249,992	$ —	$ 2,812			$ 2,812
Moffitt performance based common stock award											91,721	$ —	$ —			$ —
Exercise of stock options											29,711	$ —	$ 105			$ 105
Stock-based compensation expense													$ 4,216			$ 4,216
Unrealized gain on available-for-sale debt securities														$ 294		$ 294
Net loss															$ (55,200)	$ (55,200)
Balance at December 31, 2023	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	23,099,335	$ 23	$ 275,521	$ (119)	$ (176,758)	$ 98,667

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

Turnstone Biologics Corp.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2023	2022
Operating Activities		
Net loss	$ (55,200)	$ (30,834)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	4,216	4,368
Loss on disposal of property and equipment	324	—
Depreciation and amortization	2,798	3,901
Impairment of long-lived assets	1,582	497
Moffitt performance-based common stock award	—	2,051
Accretion of premium on short term investments	(2,059)	(98)
Change in fair value of contingent consideration liability	109	7,019
Changes in operating assets and liabilities:		
Accounts receivable - collaboration agreement	8,534	(2,013)
Prepaid expenses	426	(197)
Other current assets	(1,063)	548
Operating lease liabilities	(87)	(1,735)
Accounts payable	(3,399)	3,407
Change in contingent consideration liability	(1,477)	—
Accrued compensation and other accrued liabilities	(1,122)	(4,879)
Other non-current assets	(437)	—
Other non-current liabilities	9	—
Deferred revenue	(19,306)	(53,097)
Net cash flows used in operating activities	(66,152)	(71,062)
Investing Activities		
Proceeds from maturities of short-term investments	82,500	49,750
Purchase of short-term investments	(109,796)	(59,512)
Proceeds from sale of property and equipment	452	—
Purchases of property and equipment	(1,249)	(5,170)
Net cash flows used in investing activities	(28,093)	(14,932)
Financing Activities		
Proceeds from issuance of common stock, net of issuance costs	77,839	—
Payment of contingent consideration related to Myst milestone	(898)	(2,813)
Proceeds from exercise of stock options	105	157
Net cash flows provided by (used in) financing activities	77,046	(2,656)
Net decrease in cash, cash equivalents and restricted cash	(17,199)	(88,650)
Cash, cash equivalents and restricted cash at beginning of the period	35,113	123,763
Cash, cash equivalents and restricted cash at end of the period	$ 17,914	$ 35,113
Supplemental Disclosure of Cash Flow Information:		
Cash paid for income taxes	100	83
Supplemental Disclosure of Non-Cash Investing and Financing Activities:		
Accretion of redeemable convertible preferred stock	39	190
Additions to ROU assets obtained from new operating leases	—	4,218
Equipment purchases included in accrued expenses	535	—
Conversion of convertible preferred stock to common stock upon closing of IPO	171,983	—
Issuance of common stock to settle Myst contingent consideration liability	2,812	5,000

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

Turnstone Biologics Corp.
Notes to the Consolidated Financial Statements

1. Nature of the Business and Basis of Presentation

Organization

Turnstone Biologics Corp. (the "Company" or "Turnstone") is a clinical stage biotechnology company focused on developing new medicines to treat and cure patients with solid tumors. Turnstone is pioneering a differentiated approach to tumor infiltrating lymphocytes ("TILs"), a clinically validated technology for treating solid tumors. The Company is developing next generation TIL therapies by selecting the most potent and tumor reactive T cells ("Selected TILs"). The Company has initiated two Phase 1 clinical trials for its lead Selected TIL product candidate, TIDAL-01, for the treatment of breast cancer, colorectal cancer, uveal melanoma and other non-cutaneous and cutaneous melanomas. The Company's headquarters are located in San Diego, California.

Reverse Stock Split

On July 14, 2023, the Company effected a 1-for-7.9872 reverse stock split ("Reverse Split") of its issued and outstanding shares of common stock and redeemable convertible preferred stock. All share and per share amounts included in the accompanying consolidated financial statements and related notes have been retroactively adjusted, where applicable, to reflect the Reverse Split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital. Shares of common stock, underlying outstanding stock options, and restricted stock were proportionately reduced and the respective exercise prices, if applicable, were proportionately increased in accordance with the terms of the appropriate securities agreements. Stockholders entitled to fractional shares as a result of the Reverse Split received a cash payment in lieu of receiving fractional shares.

Initial Public Offering

On July 25, 2023, the Company completed its initial public offering ("IPO") pursuant to which it issued and sold an aggregate of 6,666,667 shares of common stock at a price to the public of $12.00 per share. Aggregate net proceeds to the Company were $68.7 million after deducting underwriting discounts and commissions of $5.6 million and other offering expenses of $5.7 million. On August 15, 2023, the underwriters exercised their option to purchase an additional 651,608 shares of common stock at $12.00 per share. Aggregate net proceeds to the Company were $7.3 million after deducting underwriting discounts and commissions of $0.5 million. Upon the closing of the IPO, all outstanding shares of redeemable convertible preferred stock automatically converted into shares of common stock. Subsequent to the closing of the IPO, there were no shares of redeemable convertible preferred stock outstanding.

In connection with the closing of the IPO, the Company filed its Amended and Restated Certificate of Incorporation which provides that the authorized capital stock of the Company is 500,000,000 shares consisting of 490,000,000 shares of common stock and 10,000,000 shares of undesignated preferred stock, both with a par value of $0.001 per share.

Sources of Liquidity

Since its inception, the Company has devoted substantially all of its efforts and financial resources to organizing and staffing the Company, business planning, raising capital, discovering product candidates and securing related intellectual property rights, and conducting research and development activities for its Selected TIL programs and product candidates. The Company does not have any products approved for sale, has not generated any revenue from product sales and has incurred overall net losses since commencement of the Company's operations, including a net loss of $55.2 million and $30.8 million for the twelve months ended December 31, 2023 and 2022, respectively. The Company has financed its operations through the issuance and sale of shares of the Company's redeemable convertible preferred stock, from collaboration revenue received pursuant to certain collaboration agreements, and most recently, with proceeds from the IPO completed on July 25, 2023 and the exercise of the underwriters option to purchase additional shares on August 15, 2023. As of December 31, 2023, the

Company had an accumulated deficit of $176.8 million. The Company expects to continue to generate significant operating losses for the foreseeable future.

The Company has evaluated and concluded there are no conditions or events, considered in the aggregate, that raise substantial doubt about its ability to continue as a going concern for a period of one year following the date these consolidated financial statements are issued and believes its existing cash and cash equivalents and short-term investments as of December 31, 2023 of $94.8 million will be sufficient to fund its operating expenses and capital expenditure requirements for at least 12 months from the date these consolidated financial statements are filed with the Securities and Exchange Commission ("SEC").

The Company intends to fund future operations and future capital funding needs through equity and/or debt financings, as well as possible asset sales, licensing transactions, and collaborations or strategic partnerships with other companies. The sale of equity or convertible debt could result in additional dilution to stockholders. The incurrence of indebtedness would result in debt service obligations and could result in operating and financial covenants that would restrict the Company's operations. The Company can provide no assurance that sufficient financing will be available on acceptable terms, if at all. If the Company is not able to secure adequate additional funding it may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, and/or suspend or curtail planned programs. Any of these actions could materially harm the Company's business.

Risks and Uncertainties

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including non-clinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance and reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

2. Summary of Significant Accounting Policies

Basis of Presentation of Consolidated Financial Information

The accompanying consolidated financial statements of the Company have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") and pursuant to the rules and regulations of the SEC. Certain prior period amounts reported in the Company's consolidated financial statements and accompanying notes have been reclassified to conform to the current period presentation. Any reference in these notes to applicable guidance is meant to refer to the authoritative accounting principles generally accepted in the United States as found in the Accounting Standard Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of these consolidated financial statements in accordance with GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. On an ongoing basis, management evaluates its estimates, including those related to accrued expenses, contingent liabilities, impairment of long-lived assets, revenue recognition, the valuation of equity-based compensation, common stock, restricted common stock, and income taxes. The Company bases its estimates on

various assumptions that the Company believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Segment Reporting

The Company has determined that it operates and manages one operating segment, which is the business of developing and commercializing therapeutics. The Company's chief operating decision maker, its chief executive officer, reviews financial information on an aggregate basis for the purpose of allocating resources.

Cash and Cash Equivalents

Cash and cash equivalents consist of checking, money market and highly liquid investments that are readily convertible to cash and that have an original maturity of three months or less from date of purchase. The carrying amounts approximate fair value due to the short maturities of these instruments.

Restricted Cash and Investments

Restricted cash consists of certificate of deposit accounts that are pledged as collateral for the Company's San Diego facility lease as of December 31, 2023 and the San Diego and New York facility leases as of December 31, 2022. Restricted cash was approximately $0.1 million and $0.4 million as of December 31, 2023 and 2022, respectively.

The Company invests its excess cash in investment grade, short-term, fixed income securities and recognizes purchased securities on the settlement date. All investments have been classified as "available-for-sale" in the consolidated balance sheets and are carried at estimated fair value based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its investments at the time of purchase and re-evaluates such designation as of each balance sheet date.

The Company assesses its available-for-sale securities under the available-for-sale security impairment model in ASC Topic 326, Financial Instruments—Credit Losses ("ASC 326") as of each reporting date in order to determine if a portion of any decline in fair value below carrying value is the result of a credit loss. The Company records credit losses in the consolidated statements of operations and comprehensive loss as credit loss expense, which is limited to the difference between the fair value and the amortized cost of the security. To date, the Company has not recorded any credit losses on its available-for-sale securities. Declines in fair value below carrying value attributable to non-credit related factors are recorded as accumulated other comprehensive loss, which is a separate component of stockholders' equity (deficit).

Realized gains and losses are reported in other income (expense), net. Interest on short-term investments is included in other income (expense), net. The Company's investments are classified as current assets which reflects management's intention to use the proceeds from sales of these securities to fund its operations, as necessary.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash and cash equivalents, investments and restricted cash. The Company's investment policy restricts cash investments to high credit quality, investment grade investments. The Company's investment policy provides guidelines and limits regarding investment type, concentration, credit quality, and maturity aimed at maintaining sufficient liquidity to satisfy operating and working capital requirements along with strategic initiatives, preserving capital, and minimizing risk of capital loss while generating returns on its investments. The Company is exposed to credit risk in the event of default by the issuer or the institutions holding the cash and cash equivalents to the extent of the amounts recorded on the balance sheets.

The Company records accounts receivable amounts invoiced to a collaborator, for which the Company has an unconditional right to consideration. For amounts to which the Company has an unconditional right to consideration but has not yet invoiced the collaborator, the Company records unbilled accounts receivable. The Company

estimates an allowance for credit losses based on the creditworthiness of its collaborator, current economic conditions and future economic conditions, as may be applicable. If a receivable is deemed to be uncollectible, the balance is charged against the allowance. As of December 31, 2023 and December 31, 2022, the Company had an accounts receivable balance of $0.2 million and $8.7 million, respectively of which Takeda accounted for 100%, and no allowance was recorded. Accounts receivable and unbilled accounts receivable are presented in accounts receivable, net on the consolidated balance sheets. During the twelve months ended December 31, 2023 and 2022, the Company did not recognize any charges for write-offs of accounts receivable.

The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts or other foreign-hedging arrangements.

Fair Value Measurements

The Company applies fair value accounting for all financial assets and liabilities and non-financial assets and liabilities that are recognized or disclosed at fair value in the consolidated financial statements on a recurring basis. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The fair value hierarchy requires that an entity maximize the use of observable inputs when estimating fair value. The fair value hierarchy includes the following three-level classification which is based on the market observability of the inputs used for estimating the fair value of the assets or liabilities being measured:

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

Level 2 – Observable inputs other than quoted prices in active markets for identical assets and liabilities, quoted prices for identical or similar assets or liabilities in inactive markets, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 – Inputs that are generally unobservable and typically reflect management's estimate of assumptions that a market participant would use in pricing the asset or liability.

Fair value accounting is applied for all financial assets and liabilities and non-financial assets and liabilities that are recognized at fair value in the consolidated financial statements on a recurring basis (at least annually). To the extent the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair values requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized as Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Investment Tax Credits

The Company claims Scientific Research and Experimental Development ("SR&ED") deductions and related investment tax credits for income tax purposes based upon management's interpretation of the applicable legislation in the *Income Tax Act* (Canada). Investment tax credits are subject to Canada Revenue Agency review and assessment of the eligibility of the Company's research expenditures. These tax credits are applied to reduce the related research and development expenses incurred in the year recognized. Actual investment tax credits received may differ from those estimated and recorded in these consolidated financial statements.

Property and Equipment

Property and equipment are recorded at cost, less accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the respective assets, which are two to three years for computer equipment and software, and five years for laboratory, office equipment and furniture. Leasehold improvements are amortized over the shorter of the useful life or the remaining term of the lease.

Revenue Recognition

The Company enters into collaboration arrangements that may include the receipt of payments for up-front license fees, success-based milestone payments, full time equivalent based payments for research services, and royalties on any future sales of commercialized products that result from the collaborations.

Effective January 1, 2017, the Company adopted the provisions of ASC Topic 606, *Revenue from Contacts with Customers* ("ASC 606"). Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, the Company performs the following five steps: (i) identification of the contract(s) with the customer, (ii) identification of the promised goods or services in the contract and determination of whether the promised goods or services are performance obligations, (iii) measurement of the transaction price, (iv) allocation of the transaction price to the performance obligations, and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect consideration it is entitled to in exchange for the goods or services it transfers to the customer.

The Company accounts for a contract with a customer that is within the scope of ASC 606 when all of the following criteria are met: (i) the arrangement has been approved by the parties and the parties are committed to perform their respective obligations, (ii) each party's rights regarding the goods or services to be transferred can be identified, (iii) the payment terms for the goods and services to be transferred can be identified, (iv) the arrangement has commercial substance and (v) collection of substantially all of the consideration to which the Company will be entitled in exchange for the goods or services that will be transferred to the customer is probable.

The Company estimates the transaction price based on the amount of consideration the Company expects for transferring the promised goods or services in the contract. The consideration may include both fixed consideration and variable consideration. At the inception of each arrangement that includes variable consideration, the Company evaluates the amount of the potential payments and the likelihood that the payments will be received. The Company utilizes either the most likely amount method or expected value method to estimate the transaction price based on which method better predicts the amount of consideration expected to be received. If it is probable that a significant revenue reversal would not occur, the variable consideration is included in the transaction price.

For arrangements that include development and regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, the Company re-evaluates the probability of achievement of such milestones and any related constraint, and if necessary, adjusts the estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue and net loss in the period of adjustment.

For sales-based royalties, including milestone payments based on the level of sales, the Company determines whether the sole or predominant item to which the royalties relate is a license. When the license is the sole or predominant item to which the sales-based royalty relates, 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).

The Company allocates the transaction price based on the estimated standalone selling price. The Company must develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. The Company utilizes key assumptions to determine the standalone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs. Certain variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration related to the satisfaction of the performance obligation and

the resulting amounts allocated to each performance obligation are consistent with the amounts the Company would expect to receive for each performance obligation.

For performance obligations, which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation in order to determine whether the combined performance obligation is satisfied over time or at a point in time. The Company determines the appropriate method of measuring progress of combined performance obligations satisfied over time for purposes of recognizing revenue determined on a contract by contract basis (*See Note 6—Agreements* for additional information). The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. 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 will recognize revenue from non-refundable, up-front 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.

The Company receives payments from customers based on billing schedules established in each contract. Up-front payments and fees are recorded as deferred revenue upon receipt or when due until the Company performs its obligations under these arrangements. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development costs consist of payroll and other personnel-related expenses, materials and supplies, preclinical expenses, manufacturing expenses, contract research and development services, and consulting costs, as well as allocations of facilities and other overhead costs. Costs of certain development activities, such as manufacturing, are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development costs. Non-refundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. Costs associated with collaboration agreements are included in research and development expenses. Assets acquired that are used for research and development and which have no alternative use are expensed to research and development costs.

Preclinical and Clinical Trial Accruals

The Company makes estimates of its accrued expenses as of each balance sheet date in the consolidated financial statements based on the facts and circumstances known at that time. Accrued expenses for preclinical studies and clinical trials are based on estimates of costs incurred and fees that may be associated with services provided by contract research organizations ("CROs"), clinical trial investigational sites and other clinical trial-related activities. Payments under certain contracts with such parties depend on factors such as successful enrollment of patients, site initiation and the completion of clinical trial milestones. In accruing for these services, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If possible, the Company obtains information regarding unbilled services directly from these service providers. However, the Company may be required to estimate these services based on other available information. If the Company underestimates or overestimates the activities or fees associated with a study or service at a given point in time, adjustments to research and development expenses may be necessary in future periods. Historically, estimated accrued liabilities have approximated actual expenses incurred. Subsequent changes in estimates may result in a material change in accruals.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Stock-Based Compensation

The Company accounts for stock-based compensation expense related to stock options and restricted stock units, ("RSUs"), by estimating the fair value on the date of grant. The Company estimates the fair value of stock options granted to employees and non-employees using the Black-Scholes option pricing model. The fair value of RSUs granted to employees is the closing price of the Company's common stock on the date of grant. The Company recognizes stock-based compensation expense, over the requisite service period, based on the vesting provisions of the individual grants. Generally, the Company issues stock-based awards with only service-based vesting conditions and records the expense for these awards using the straight-line method. The Company accounts for forfeitures when they occur.

The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (a) the expected stock price volatility, (b) the expected term of the award, (c) the risk-free interest rate and (d) expected dividend yields. Due to the lack of a public market for the Company's common stock until July 21, 2023, and lack of company- specific historical and implied volatility data, the Company has based its computation of expected volatility on the average historical volatility of a representative group of public companies with similar characteristics to the Company, including stage of product development and life science industry focus. The historical volatility is calculated based on a period of time commensurate with the expected term. The Company uses the simplified method as prescribed by the U.S. Securities and Exchange Commission Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock.

Determination of Fair Value of Common Stock

After the Company's IPO in July 2023, the fair value of common stock is determined using the closing price of the Company's common stock on the Nasdaq Global Select Market. Prior to the IPO, there were significant judgments and estimates inherent in the determination of the fair value of the Company's common stock. These estimates and assumptions include a number of objective and subjective factors, including, among other things, external market conditions, the prices at which the Company sold shares of its convertible preferred stock, the superior rights and preferences of securities senior to its common stock at the time of, and the likelihood of, achieving a liquidity event, such as an initial public offering or sale of the Company. The approach to estimating the fair market value of common stock is consistent with the methods outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held Company Equity Securities Issued as Compensation ("Practice Aid").

In valuing the Company's common stock prior to the IPO, the equity value of the business was determined using the backsolve method, a form of the subject company transaction method, wherein the equity value for a privately held company is derived from a recent transaction in the company's own securities. The value is then allocated using the hybrid method allocation methodology. For grants made prior to September 30, 2018, in accordance with the Practice Aid, the Company determined the option pricing method ("OPM"), was the most appropriate method for determining the fair value of the Company's common stock based on its stage of development and other relevant factors. For grants made subsequent to September 30, 2018 but prior to the IPO, the Company used a hybrid method, which is a hybrid between the OPM and the probability-weighted expected return method ("PWERM"). The hybrid method is a combination of the PWERM and OPM. The OPM allocates the overall Company value to the various share classes based on differences in liquidation preferences, participation rights, dividend policy and conversion rights, using a series of call options. The call right is valued using a Black-Scholes option pricing model. The PWERM employs additional information not used in the OPM, including various market approach calculations depending upon the likelihood of various discrete future liquidity scenarios, such as an initial public offering or sale of the Company, as well as the probability of remaining a private company. In a hybrid method, various exit scenarios are analyzed. A discount for lack of marketability of the Company's common stock was then applied to arrive at an indication of value for the common stock.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable, including evaluating the impact of the overall micro- and macro-economic conditions on the carrying value of its long-lived assets, including property and equipment and operating lease assets. During the twelve months ended December 31, 2023, the Company's stock price and resulting market capitalization experienced a significant, sustained decline. Accordingly, the Company assessed our long-lived assets, including property and equipment and operating lease assets for impairment. Recoverability of these assets is determined by comparing the forecasted undiscounted net cash flows of the operation to which the assets relate to the carrying amount. If the operation is determined to be unable to recover the carrying amount of its assets, then these assets are written down first to fair value Fair value is determined based on discounted cash flows or appraised values, depending on the nature of the assets.

The Company recognized long-lived asset impairment charges of $1.6 million and $0.5 million for the years ended December 31, 2023 and 2022, respectively (*See Note 4—Property and Equipment, Net and Note 11—Leases* for additional information).

Redeemable Convertible Preferred Stock

The Company records all proceeds from redeemable convertible preferred stock ("Preferred Stock") net of issuance costs. The Company classifies Preferred Stock outside of stockholders' equity (deficit) due to certain events that are outside of the Company's control, including sale or transfer of control of the Company, or redemption upon the election of the required majority of the Preferred Stockholders any time after June 29, 2026, as holders of the Preferred Stock could cause redemption of the shares in these situations. The Company adjusts the carrying values of the Preferred Stock to the ultimate redemption values over the period from issuance to the earliest redemption date. Upon the closing of the IPO, all of the outstanding shares of Preferred Stock automatically converted into shares of common stock in a 1-for-7.9872 reverse stock split.

Income Taxes

The Company accounts for the effect of income taxes in its consolidated financial statements using the asset and liability method in accordance with ASC Topic 740, Income Taxes ("ASC 740"). This process involves estimating actual current tax liabilities together with assessing the impact of carryforward and temporary differences resulting from the differing treatment of items such as depreciation for tax and accounting purposes. These differences result in deferred tax assets and liabilities which are measured using enacted tax rates expected to apply to taxable income in the year in which those temporary differences are expected to reverse.

The Company regularly assesses the likelihood that the deferred income tax assets will be realized. A valuation allowance to reduce the deferred tax assets to the amount that the Company believes is more likely than not to be realized is established based on their judgement of all available positive and negative evidence. The assessment is completed on a taxing jurisdiction basis for each tax-paying component and takes into account a number of types of evidence, including:

- the nature and history of current or cumulative financial reporting income or losses;
- sources of future taxable income;
- the anticipated reversal or expiration dates of deferred tax assets; and
- tax planning strategies.

The Company has established a valuation allowance to offset its gross deferred tax assets as of December 31, 2023 and 2022 due to the uncertainty of realizing future tax benefits primarily related to net operating loss carryforwards and income tax credits in Canada.

The Company applies ASC 740-10 Income Taxes which requires a two-step approach to recording a tax benefit in the consolidated financial statements. The first step requires an evaluation of the tax position to determine whether it is "more likely than not", based on the technical merits, that it will be sustained on audit. Provided that

the tax position satisfies the recognition step, the Company then measures and records the position at the largest amount of tax benefit that is greater than 50 percent likely of being realized upon settlement of the audit. The Company considers many factors when evaluating and estimating its tax positions and tax benefits, which may require periodic adjustments and may not accurately anticipate actual outcomes. The Company recognizes accrued interest and penalties related to unrecognized tax benefits. There were no accrued interest and penalties as of December 31, 2023.

Net Loss Per Share

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period.

Diluted net loss per share is computed by giving effect to all potentially dilutive securities outstanding for the period using the treasury stock method or the if-converted method based on the nature of such securities. For periods in which the Company reports net losses, diluted net loss per common share attributable to common stockholders is the same as basic net loss per common share attributable to common stockholders, because potentially dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Prior to the Company's IPO, the Company applied the two-class method to compute basic and diluted net loss per share because it had issued redeemable convertible preferred stock that met the definition of participating securities. The two-class method determined net loss per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method required earnings available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to share in the earnings as if all earnings for the period had been distributed. During periods of loss, there was no allocation required under the two-class method since the participating securities do not have a contractual obligation to fund the losses of the Company.

Foreign Currency

The accumulated other comprehensive loss on the balance sheet includes foreign currency translation adjustments through December 31, 2015 recorded in connection with the change in functional currency from the Canadian dollar to the U.S. dollar. Gains or losses resulting from transactions denominated in foreign currencies are recorded as a component of other income or expense, within the consolidated statements of operations and comprehensive loss.

Leases

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present. Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not readily determinable. As such, the Company utilizes its incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received.

The Company has elected to combine lease and non-lease components as a single component. The lease expense is recognized over the expected term on a straight-line basis. The lease term for all of the Company’s leases includes the non-cancellable period of the lease plus any additional periods covered by either a Company option to extend (or not to terminate) the lease that the Company is reasonably certain to exercise. Variable lease payments associated with the Company’s leases are recognized when the event, activity, or circumstance in the lease agreement on which those payments are assessed occurs. Variable lease payments are presented in the Company’s consolidated statements of operations and comprehensive loss in the same line item as expense arising from fixed lease payments for operating leases. Balances related to operating leases are recognized on the consolidated balance sheets as right-of-use assets, operating lease liabilities, current and operating lease liabilities, non-current.

Deferred Offering Costs

The Company had deferred offering costs, related to its recently completed IPO, consisting of legal, accounting and other fees and costs directly attributable to the Company's IPO and are included with other assets, noncurrent in the consolidated balance sheets until the completion of the IPO. The deferred offering costs were offset against the proceeds received upon the completion of the IPO. As such, there were no deferred offering costs as of December 31, 2023. As of December 31, 2022, the Company recorded $1.9 million of deferred offering costs.

Contingent Consideration

Consideration paid related to the Myst Merger Agreement (*see Note 7 - Asset Acquisition* for additional information) may include potential future payments that are contingent upon the Company achieving certain milestones in the future. Contingent consideration liabilities are measured at their estimated fair value as of the date of the consolidated balance sheets using a probability-based income approach based on the monetary value of the milestone payment discounted for the likelihood of achieving the milestone and a present value factor based on the timing of when the milestone is expected to be achieved. Contingent consideration liabilities expected to be settled within 12 months after the balance sheet date are presented in current liabilities, with the non-current portion recorded under other liabilities, non-current in the consolidated balance sheets. Changes in the fair value of the contingent consideration are recorded as research and development expenses in the consolidated statement of operations and comprehensive loss.

Recently Adopted Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments—Credit Losses (Topic 326)—Measurement of Credit Losses on Financial Instruments, which has been subsequently amended by ASU No. 2018-19, ASU No. 2019-04, ASU No. 2019-05, ASU No. 2019-10, ASU No. 2019-11 and ASU No. 2021-03 ("ASU 2016-13"). The provisions of ASU 2016-13 modify the impairment model to utilize an expected loss methodology in place of the currently used incurred loss methodology and require a consideration of a broader range of reasonable and supportable information to inform credit loss estimates. ASU 2016-13 was effective for the Company on January 1, 2023. The adoption did not have a material impact on the consolidated financial statements.

Recently Issued Accounting Pronouncements

In August 2020, the FASB issued ASU No. 2020-06, Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging Contracts in Entity's Own Equity (Subtopic 815-40) ("ASU 2020-06"), which reduces the number of accounting models for convertible debt instruments and convertible preferred stock as well as amends the derivatives scope exception for contracts in an entity's own equity. ASU 2020-06 is effective for the Company on January 1, 2024, with early adoption permitted. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial statements and related disclosures.

In November 2023, the FASB issued ASU No. 2023-07, Segment Reporting (Topic 280)—Improvements to Reportable Segment Disclosures ("ASU 2023-07"). ASU 2023-07 requires that an entity disclose significant segment expenses impacting profit and loss that are regularly provided to the chief operating decision maker. The update is required to be applied retrospectively to prior periods presented, based on the significant segment expense categories identified and disclosed in the period of adoption. The amendments in ASU 2023-07 are required to be adopted for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024. Early adoption is permitted. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial statements and related disclosures.

In December 2023, the FASB issued ASU No. 2023-09, Income Taxes (Topic 740)—Improvements to Income Tax Disclosures ("ASU 2023-09"). ASU 2023-09 requires that an entity disclose specific categories in the effective tax rate reconciliation as well as provide additional information for reconciling items that meet a quantitative threshold. Further, ASU 2023-09 requires certain disclosures of state versus federal income tax expense and taxes paid. The amendments in ASU 2023-09 are required to be adopted for fiscal years beginning after December 15, 2024. Early adoption is permitted for annual financial statements that have not yet been issued. The amendments should be applied on a prospective basis although retrospective application is permitted. The Company

is currently evaluating the potential impact that this standard may have on its consolidated financial statements and related disclosures.

3. Fair Value of Financial Assets and Liabilities

As of December 31, 2023 and 2022, the Company's restricted cash which is maintained as collateral in connection with its New York and San Diego facility leases, (See Note 2 – Summary of Significant Accounting Policies for additional information) are valued using Level 1 inputs. The Company's highly liquid money market funds included within cash equivalents, restricted cash and U.S. treasury securities are valued using Level 1 inputs. The Company classifies its federal agency securities as Level 2. There were no transfers in or out of Level 1 and Level 2 during the periods presented. U.S. treasury securities are bonds issued by the U.S. government and are fully backed by the U.S. government. Given the frequency at which U.S. treasury securities trade and the accessibility of observable, quoted prices for such assets in active markets, they are recognized as Level 1 assets. Federal agency securities are bonds and notes issued by government-sponsored enterprises, including Fannie Mae, Freddie Mac and the Federal Home Loan Bank. Since Federal agency securities typically do not trade as frequently as U.S. government agency securities and no exchange exists to price such investments, they are recognized as Level 2 assets.

The Company had $0.9 million and $6.0 million in contingent consideration liabilities as of December 31, 2023 and 2022, respectively, related to the Myst Merger Agreement. The contingent consideration balances are comprised of one potential milestone payment as of December 31, 2023 and two separate potential milestone payments as well as the remaining unpaid liability of $2.2 million from the milestone achievement as of December 31, 2022 with each measured at fair value (See Note 7—Asset Acquisition for additional information). The fair value of the contingent consideration is estimated based on the monetary value of the milestone discounted for the likelihood of achieving the milestone and a present value factor based on the timing of when the milestone is expected to be achieved. The value for the contingent consideration balance is based on significant inputs not observable in the market which represents a Level 3 measurement within the fair value hierarchy. There were no transfers in or out of Level 3 during the periods presented.

The following tables represent a summary of the financial assets and liabilities that are measured on a recurring basis at fair value *(in thousands)*:

	December 31, 2023			
	Level 1	Level 2	Level 3	Fair Value
Financial assets:				
Money market funds	$ 15,635			$ 15,635
Restricted cash[1]	116	—	—	116
U.S. government and agency securities[2]	76,979	—	—	76,979
Total financial assets	$ 92,730	$ —	$ —	$ 92,730
Financial liabilities:				
Contingent consideration[3]	$ —	$ —	$ 916	$ 916
Total financial liabilities	$ —	$ —	$ 916	$ 916

	December 31, 2022			
	Level 1	Level 2	Level 3	Fair Value
Financial assets:				
Money market funds	$ 9,238	$ —	$ —	$ 9,238
Restricted cash[1]	382	—	—	382
U.S. government and agency securities[2]	30,649	16,681	—	47,330
Total financial assets	$ 40,269	$ 16,681	$ —	$ 56,950
Financial liabilities:				
Contingent consideration[3]	$ —	$ —	$ 5,994	$ 5,994
Total financial liabilities	$ —	$ —	$ 5,994	$ 5,994

(1) Restricted cash serves as deposits for the Company's San Diego office lease as of December 31, 2023 and New York and San Diego office leases as of December 31, 2022.

(2) Included in short-term investments on the consolidated balance sheets and are classified as available-for sale debt securities.
(3) Contingent consideration related to the Myst Merger Agreement.

The following significant unobservable inputs were used in the valuation of the contingent consideration payable to the sole common stockholder of Myst pursuant to the Myst Merger Agreement:

Contingent Consideration Liability	Fair Value as of December 31, 2023	Valuation Technique	Unobservable Input	Range
	(in thousands)			
Milestone payment for first registrational study (see *Note 7 - Asset Acquisition* for additional information)	$ 916	Discounted cash flow	Likelihood of occurrence	10%
			Discount rate	25%
			Expected term (in years)	3.5

Contingent Consideration Liability	Fair Value as of December 31, 2022	Valuation Technique	Unobservable Input	Range
	(in thousands)			
Milestone payments	$ 5,994	Discounted cash flow	Likelihood of occurrence	20% - 100%
			Discount rate	22%
			Expected term (in years)	0.25 - 2.75

The following table reflects the activity for the Company's contingent consideration, measured at fair value using Level 3 inputs (*in thousands*):

Contingent consideration at December 31, 2022	$ 5,994
Changes in the fair value of contingent consideration	109
Cash payment of Myst milestone	(2,375)
Equity issuance related to milestone achievement	(2,812)
Contingent consideration at December 31, 2023	916

The following tables show the Company's cash, cash equivalents and available-for-sale securities by significant investment category *(in thousands)*:

	December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Level 1: Money market funds	$ 15,635	$ —	$ —	$ 15,635
Restricted cash	116	—	—	116
U.S. government securities	76,875	104	—	76,979
Total financial assets	$ 92,626	$ 104	$ —	$ 92,730
Classified as:				
Cash and cash equivalents				$ 15,635
Restricted cash				116
Short-term investments				76,979
				$ 92,730

	December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Level 1: Money market funds	$ 9,238	$ —	$ —	$ 9,238
Restricted cash	382	—	—	382
U.S. government securities	30,761	—	(112)	30,649
Level 2: U.S. agency securities	16,759	—	(78)	16,681
Total financial assets	$ 57,140	$ —	$ (190)	$ 56,950
Classified as:				
Cash and cash equivalents				$ 9,238
Restricted cash				382
Short-term investments				47,330
				$ 56,950

As of December 31, 2023, 0 of 28 of our available-for-sale debt securities were in a gross unrealized loss position. As of December 31, 2022, 23 out of 24 of our available-for-sale debt securities were in an aggregate gross unrealized loss position of $0.2 million with an aggregate fair value of $45.3 million. While short-term investments are available-for-sale, it is not more likely than not that the Company will be required to sell the investments before recovery of their amortized cost bases, which may be maturity. All short-term investments currently held have maturities of less than one year.

The Company reviews short-term investments for impairment during each reporting period. Credit losses are recognized up to the amount equal to the difference between the fair value and the amortized cost basis and recorded as an allowance for credit losses in the consolidated balance sheets with a corresponding adjustment to earnings. Unrealized losses that are not related to credit losses are recognized in accumulated other comprehensive loss. There were no unrealized losses in the Company's investment portfolio at December 31, 2023. Unrealized losses were not significant for the investments held in the Company’s portfolio as of December 31, 2022 and the Company considered the decline in market value for these securities to be primarily attributable to economic and market conditions rather than credit-related factors. The Company considered the risk-profile of the counterparties under ASU 2016-13, noting that any credit risk associated with such entities is either zero or near zero. There were no impairment losses or expected credit losses related to its short-term investments during the twelve months ended December 31, 2023 and 2022.

4. Property and Equipment, Net

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

	December 31, 2023	December 31, 2022
Computer equipment and software	$ —	$ 376
Laboratory equipment	11,043	12,901
Furniture	690	758
Leasehold improvements	1,308	1,308
	13,041	15,343
Less: Accumulated depreciation and amortization	(6,689)	(5,619)
Total property and equipment, net	$ 6,352	$ 9,724

Property and equipment depreciation and amortization expense for the twelve months ended December 31, 2023 and 2022, was $2.8 million and $2.2 million, respectively.

The gain (loss) on disposal of property and equipment was ($0.3) million and $0.1 million for the twelve months ended December 31, 2023 and 2022, respectively.

During the twelve months ended December 31, 2023, the Company's stock price and resulting market capitalization experienced a significant, sustained decline. Accordingly, the Company assessed our long-lived assets, including its property, plant and equipment and operating lease assets for impairment. For its property and equipment, the Company performed a recoverability test by comparing the future cash flows attributable to the property and equipment to the carrying value of the assets. Based on this evaluation, the Company determined that the property and equipment with a carrying value of $7.9 million was no longer recoverable. As a result, the Company recognized an impairment charge of $1.6 million which was calculated as the difference between fair value of the assets and its carrying value. The fair value was based on the indirect cost approach which considers the cost of constructing a new asset less depreciation and obsolescence. the fair value ws determined using level 3 inputs. The impairment charge was recorded as research and development expenses in the consolidated statement of operations and comprehensive loss for the twelve months ended December 31, 2023.

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following *(in thousands):*

	December 31, 2023	December 31, 2022
Research and development expense	$ 5,675	$ 6,688
Professional and consulting expense	641	1,170
Compensation	3,593	2,366
Contingent consideration, current	—	3,791
Other current liabilities	—	272
Total accrued expenses and other current liabilities	$ 9,909	$ 14,287

6. Agreements

Takeda Pharmaceutical Company Limited

Collaboration Agreement

In November 2019, the Company entered into a discovery, collaboration and license agreement ("Takeda Agreement") with Millennium Pharmaceuticals, Inc. (also known as Takeda Oncology), a wholly owned subsidiary of Takeda Pharmaceutical Company Limited (Takeda). Under the Takeda Agreement, the Company agreed to collaborate with Takeda to co-develop and co-commercialize TBio-6517 (also known as RIVAL-01) ("Development Program") and to conduct discovery programs to identify additional novel product candidates based on its vaccinia virus platform for independent development ("Discovery Program").

Under the Takeda Agreement, the Company granted Takeda and its affiliates a worldwide, irrevocable, non-transferable, co-exclusive, sublicensable license under certain of the Company's know-how and patent rights ("Turnstone Technology") to make, use, sell, offer for sale, develop, manufacture, and commercialize, or otherwise exploit TBio-6517 ("Licensed Compound") and products containing TBio-6517 ("Takeda Licensed Products") in all fields. Takeda granted the Company and the Company's affiliates an irrevocable, non-transferable, non-exclusive, sublicensable license under certain know-how and patent rights of Takeda ("Takeda Technology") to make, use, sell, offer for sale, develop, manufacture, and commercialize, or otherwise exploit the Licensed Compound and Takeda Licensed Products in all fields in accordance with joint development, commercialization, and medical affairs plans under the Takeda Agreement. Under the Takeda Agreement, the Company also granted to Takeda and its affiliates a worldwide, non-transferable, non-exclusive, sublicensable license under Turnstone Technology to conduct joint discovery and research activities in all fields in accordance with joint research and discovery plans. Under the Takeda Agreement, Takeda granted the Company a license to Takeda Technology to conduct discovery and research activities in all fields in accordance with joint research and discovery plans. The Company also granted to Takeda and its affiliates an exclusive option to obtain a worldwide, irrevocable, non-transferable, exclusive, sublicensable license under Turnstone Technology to make, use, sell, offer for sale, develop, manufacture, and commercialize, or otherwise exploit (i) selected discovery virus candidates generated and evaluated by the parties under a joint discovery program ("Selected Discovery Candidates"), and (ii) any corresponding licensed products containing a Selected Discovery Candidate ("Licensed Discovery Products"). Takeda may exercise this option with

respect to two virus candidates and within a specified option exercise period. The Company granted Takeda and its affiliates a non-exclusive, perpetual, irrevocable, worldwide, sublicensable and fully paid-up license under certain of the Company's know-how and patents relating to manufacturing improvements developed under the Takeda Agreement solely for use in connection with the manufacture of products that do not comprise or incorporate, and that are not based on, an oncolytic virus. Takeda granted the Company and the Company's affiliates a non-exclusive, perpetual, irrevocable, worldwide, sublicensable and fully paid-up license under certain of Takeda's know-how and patents relating to manufacturing improvements developed under the Takeda Agreement solely for use in connection with the manufacture of any and all products. With respect to discovery virus candidates for which Takeda does not exercise its option, Takeda granted the Company a non-exclusive, perpetual, worldwide, sublicensable and royalty-bearing license under certain of its know-how and patents that is necessary or reasonably useful for the exploitation of such declined discovery virus candidates ("Declined Candidate License").

Responsibilities for the development of Licensed Compounds and Takeda Licensed Products are delineated pursuant to a joint development plan under the terms of the Takeda Agreement. The Company will be responsible for all activities under the joint development plan prior to completion of a Phase 2a clinical trial and Takeda will be responsible for all activities in the joint development plan upon and after completion of the Phase 2a clinical trial. Responsibilities relating to manufacturing, medical affairs, and commercialization of Licensed Compounds and Takeda Licensed Products are delineated pursuant to a manufacturing working plan, joint medical affairs plan and joint commercialization plan, respectively. The Company has the right to reduce or opt-out of its share of responsibilities for costs and expenses of certain development or commercialization activities for the Takeda Licensed Compounds and Takeda Licensed Products. Responsibilities for the discovery and research of Selected Discovery Candidates are delineated pursuant to joint discovery and research plans under the terms of the Takeda Agreement.

Under the Takeda Agreement, Takeda paid the Company a non-refundable payment of $50.0 million in November 2019 and an additional non-refundable payment of $30.0 million in April, 2020, for the option to license up to two Selected Discovery Candidates, with additional consideration of $15.0 million to be paid by Takeda to the Company for each exercise of such option.

Under the Takeda Agreement, the Company has the right to reduce its share of funding obligations with respect to development activities for the Licensed Compound and Takeda Licensed Products (the "Development Opt-Down Right"), or to opt-out of all further funding obligations with respect to development activities for the Licensed Compound and Takeda Licensed Products (the "Development Opt-Out Right"). Unless and until the Company exercises the Development Opt-Down Right, the parties will share evenly in any operating profits or losses with respect to joint development activities, joint medical affairs activities, and joint commercialization activities. If the Company exercises its Development Opt-Down Right, then starting from the effective date of the exercise of the right, Takeda will bear (and be entitled to) 70% and the Company will bear (and be entitled to) 30% of the operating profits or losses with respect to joint development activities, joint medical affairs activities, and joint commercialization activities. Takeda is obligated to pay the Company (i) up to $200.0 million in aggregate upon achievement of certain clinical and regulatory milestones for the first Takeda Licensed Product to achieve the applicable development milestone event, (ii) up to $150.0 million in aggregate for one-time payments upon achievement of certain sales milestones for each Takeda Licensed Product, (iii) up to $240.0 million in aggregate (if Takeda exercises both options to Selected Discovery Candidates) upon achievement of certain clinical and regulatory milestones for the first Takeda Licensed Discovery Product to achieve applicable development milestone events, and (iv) up to $300.0 million in aggregate (if Takeda exercises both options to Selected Discovery Candidates) for one-time payments upon achievement of certain sales milestones for a Licensed Discovery Product. If the Company exercises its Development Opt-Out Right for the Takeda Licensed Products, then in lieu of the profit and loss share arrangement described above, the Company is entitled to receive tiered low- to high- teen percentage royalties on net sales of all Takeda Licensed Products by the Company or the Company's sublicensees during the royalty term, which commences on the first commercial sale of a Takeda Licensed Product in a country and ends on the later of the expiration of all licensed patents covering such Licensed Product in such country or ten years after the date of the first commercial sale in such country ("Royalty Term"). For Licensed Discovery Products, the Company is entitled to receive tiered high-single digit to low-teen percentage royalties on net sales of all Licensed Discovery Products by the Company or the Company's sublicensees during the Royalty Term. Royalty payments are subject to customary reductions.

Takeda has the right to terminate for convenience as follows: (i) prior to the expiration of the option exercise period related to a Discovery Virus Candidate, Takeda may terminate the Takeda Agreement related to such Discovery Virus Candidate and the Discovery Program with 90 days' notice, (ii) prior to any commercial sale, Takeda may terminate the Takeda Agreement either in its entirety or on a compound-by-compound or region-by-region basis, with six months' notice and (iii) after a commercial sale, Takeda may terminate the Takeda Agreement either in its entirety or on a compound-by-compound or region-by-region basis, with 12 months' notice.

Termination of Development Program

On June 13, 2022, Takeda provided six months' written notice to terminate the Development Program in accordance with its termination for convenience rights, with such termination being effective as of December 13, 2022. During the six months' notice period, the Company was obligated to continue providing the necessary Development Program services to wind down the program. Upon the effective termination date of December 13, 2022, Takeda's co-exclusive license to TBio-6517 terminated and the Company is no longer obligated to pursue development of TBio-6517.

Termination of Discovery Program

On January 6, 2023, Takeda provided six months' written notice to terminate the remainder of the Takeda Agreement, with such termination being effective as of July 6, 2023 ("Effective Termination Date"). On the Effective Termination Date, all options and licenses granted under the Takeda Agreement terminated (except for the Declined Candidate License) and Takeda granted the Company a non-exclusive license under the patent rights and know-how controlled by Takeda as of the Effective Termination Date necessary for the Company to exploit the Licensed Compound and Takeda Licensed Products in the form existing as of the Effective Termination Date for any use worldwide, subject to a royalty to be agreed upon by Takeda and the Company. As of March 31, 2023, the Company ceased all work under the Takeda Agreement and there were no remaining estimated services associated with the obligations under the Takeda Agreement as of the effective termination date of July 6, 2023.

Accounting Analysis

The Company assessed the promised goods and services under the Takeda Agreement in accordance with ASC 606, and determined that, at inception, the Takeda Agreement includes the following performance obligations: (i) research, development and manufacturing services under the Development Program for the completion of clinical trials through Phase 2a for RIVAL-01 and a co-exclusive license to exploit RIVAL-01 ("Development Program Performance Obligation"); and (ii) research and development services under the Discovery Program to identify and optimize four Selected Discovery Candidates for further development ("Discovery Program Performance Obligation"). The individual promises under the Development Program including research, development, manufacturing for clinical trials, and the co-exclusive license to RIVAL-01 are not individually distinct as they represent inputs into a combined output of advancing RIVAL-01 through the Phase 2a clinical trial. Therefore, all promises under the Development Program represent a single performance obligation. Similarly, the research and development services under the Discovery Program represent a single research program aimed at generating four Selected Discovery Candidates and therefore represents a single performance obligation. The Development Program promises are distinct from the promises under the Discovery Program, as the benefits under each program are separately identifiable. Each program has a separate work plan and the promises to be provided under the Development Program do not relate to the promises to be provided under the Discovery Program.

The Company concluded that Takeda's license options under the Discovery Program do not represent material rights, and therefore are not performance obligations, as the Company is entitled to an additional $15.0 million payment for each license option exercised, which approximates the estimated standalone selling price of the underlying license.

- Fixed consideration of $80.0 million including a non-refundable up-front payment of $50.0 million in November 2019 and another non-refundable payment of $30.0 million that was due on April 1, 2020 and received in April 2020.

- Variable consideration related to the expense sharing under the Development Program. These amounts are determinable based on the Development Program plan and budget, and the Company has a contractual right to the payment of costs incurred under the agreed upon plan. Consistent with the expected value method, the Company estimated that it will receive $58.6 million under the expense sharing through the completion of the Phase IIa clinical trial. The Company has concluded that these amounts do not require a constraint and are included in the transaction price at inception. The Company has evaluated this estimate at each reporting date and updated the estimate based on information available.
- Variable consideration for the development milestones under the Development Program. The Company uses the most likely amount method to value this variable consideration as there are only two possible outcomes of achieving the individual milestones. Under the Development Program, the first milestone of $20.0 million is due upon acceptance of the IND by the FDA. At inception, the Company concluded that achievement of this milestone was highly probable and therefore the $20.0 million was included in the transaction price and was received in March 2020. The second milestone of $15.0 million under the Development Program is due upon the initiation of the first Phase 2 clinical trial for a licensed product. The Company has determined that the most likely amount is $15.0 million, however, the Company will not include this $15.0 million milestone in the transaction price until it becomes probable that a significant reversal of cumulative revenue will not occur.

Additional consideration to be paid to the Company includes development and sales milestones, profit and loss share, royalties and option exercise payments. These additional payments are achievable only after the completion of the Phase 2a clinical trial under the Development Program or exercise of the license options under the Discovery Program and therefore are excluded from the transaction price. Additionally, Takeda's equity purchase commitments of up to $20.0 million are at fair value and therefore no non-cash consideration has been included as a component of the transaction price.

The Company allocated the transaction price to the separate performance obligations based on their relative standalone selling prices. The Company determined the standalone selling price of the Development Program Performance Obligation based on the costs incurred to develop RIVAL-01 plus the estimated costs to perform the research, development and manufacturing services through the completion of the Phase 2a clinical trial, inclusive of a reasonable profit margin. The Company determined the standalone selling price of the Discovery Program Performance Obligation based on the estimated costs to discover and research four Selected Discovery Candidates, inclusive of a reasonable profit margin. Significant inputs used to determine the standalone selling prices of the performance obligations include the length of time required, the internal hours expected to be incurred on the services, and the amount of third-party expenses that will be incurred to complete the performance obligations.

The Company recognizes the amounts associated with these performance obligations on a proportional performance basis over the contract term using input-based measurements of total cost of research and development incurred to estimate the proportion performed as compared to the estimated total cost and remeasures its progress towards completion at the end of each reporting period.

As of December 31, 2021, the transaction price was updated to $192.6 million to reflect an increase in the variable consideration related to the expense sharing under the Development Program from $58.6 million at inception to $92.6 million.

The Company determined that the notice of termination on June 13, 2022, represented a modification of the arrangement under ASC 606 and that the transaction price should be updated and re-allocated to the Development Program Performance Obligation and the Discovery Program Performance Obligation based on their standalone selling prices, as follows:

Performance Obligations	Price Pre-Modification	Price at Modification
Development Program	$166.3 million	$134.3 million
Discovery Program	$26.3 million	$21.2 million
Total	$192.6 million	$155.5 million

Additionally, the Company updated its measure of progress for each performance obligation as of the modification date and recorded a cumulative adjustment that increased collaboration revenue by $31.6 million on the partially satisfied remaining performance obligations, as the remaining services to be performed under each of the performance obligations are not distinct from the services prior to the modification.

Costs incurred relating to the Takeda Agreement consist of internal and external research and development costs, which primarily include salaries and benefits, lab supplies, and preclinical research studies. All of these costs are included in research and development expenses in the Company's consolidated statements of operations and comprehensive loss during the twelve months ended December 31, 2023 and 2022.

The deferred revenue balance in connection with the Takeda Agreement as of December 31, 2023 and 2022 was $0.0 million and $19.3 million, respectively, which is classified as either current or noncurrent in the accompanying consolidated balance sheets based on the periods the performance obligations are expected to be performed. The Company recognized the remaining deferred revenue balance during the three months ended March 31, 2023 as the Company concluded that there were no remaining estimated services to be performed associated with the obligations under the Takeda Agreement. The Company recognized collaboration revenue related to the Takeda Agreement for the twelve months ended December 31, 2023 and 2022 of $19.3 million and $73.3 million, respectively. Receivables related to reimbursable costs expected to be received from Takeda for research and development services performed under the Development Program at December 31, 2023 and 2022 were $0.2 million and $8.7 million, respectively.

H. Lee Moffitt Cancer Center

Master Collaboration Agreement

In January 2021, the Company entered into an amended and restated master collaboration agreement (the "Moffitt Agreement"), with Moffitt, to amend a then-existing master collaboration agreement from November 2019, as amended March 2020, between Moffitt and the Company's now wholly-owned subsidiary, Myst Therapeutics LLC, with the intent to continue to work collaboratively in the research of cancer immunotherapies.

Each party granted the other party a right to use its research materials for performance of the research plans agreed to by the parties (the "Research Plans"). Each party granted the other party a non-exclusive, worldwide, sublicensable, perpetual, irrevocable, royalty-free license under all inventions invented in performance of a Research Plan and invented jointly by the Company and Moffitt (the "Joint Inventions") (with certain exclusions) to make, use, sell, offer for sale, import products and services and/or otherwise practice such inventions.

The Company granted Moffitt a royalty free, non-sublicensable, non-transferable, perpetual, non-exclusive license to use and practice certain inventions invented solely by the Company in the performance of a Research Plan for its internal non-commercial research purposes.

Moffitt granted the Company (i) a royalty-free, sublicensable, non-transferable, perpetual, non-exclusive license to use and practice certain inventions invented solely by Moffitt in the performance of a Research Plan ("Moffitt Inventions"), (a) for internal, non-commercial research purposes outside the field of ACT and/or (b) to research, develop, make, use, sell, offer to sell, or import products and/or services in the field of ACT and (ii) a royalty free, sublicensable, non-transferable, perpetual, non-exclusive license to use and practice certain inventions invented in performance of a Research Plan or through the use of specified Moffitt research materials.

Moffitt granted the Company an option to obtain, with terms to be negotiated in good faith under commercially reasonable terms, a royalty-bearing, sublicensable exclusive license in the Moffitt Inventions, the TCR Inventions, and/or Moffitt's interest in Joint Inventions. The Company can exercise this option at any time within six months after Moffitt informs the Company of any new invention, and upon the Company's exercise, the parties will have a period of six months to negotiate the terms of such exclusive license.

The Moffitt Agreement will expire upon the later of (i) four years from the effective date of the Moffitt Agreement or (ii) the termination or expiration of all Research Plans in effect under the Moffitt Agreement, unless

extended upon mutual written agreement of the parties. Either party may terminate the Moffitt Agreement for cause upon any uncured breach by the other party or upon the insolvency of the other party.

Moffitt Alliance Agreement

In June 2022, the Company entered into a life science alliance agreement with Moffitt (the "Alliance Agreement"), in order to further expand the Company's relationship and support the Company's existing agreements with Moffitt (the "Underlying Agreements"). Pursuant to the Alliance Agreement, the Company will have priority access to Moffitt's scientific research, manufacturing, and clinical capabilities for the development of novel TIL therapies, including expedited clinical trial activation, enhanced patient screening and data sharing, access to Moffitt's cellular therapies research and development infrastructure, expanded molecular data sets and biospecimens for research, and allocated cGMP manufacturing capacity for the Company's product candidates.

Under the Alliance Agreement, the Company is obligated to use commercially reasonable efforts to further develop TIL Products, to manufacture TIL Products, to obtain regulatory approval for at least one TIL Product in the United States and to commercialize TIL Products in all countries in which regulatory approval for a TIL Product has been obtained. For purposes of the Alliance Agreement, TIL Product means any pharmaceutical, biopharmaceutical, or biotechnology TIL product that has been developed by us or Moffitt and is advanced into clinical development under an IND sponsored by Moffitt.

Pursuant to the Alliance Agreement, the Company agreed to pay to Moffitt a total amount of at least $17.5 million (the "Alliance Funding Amount"), for research, development and manufacturing related services that will be paid equally over five years on June 1st of each year starting on June 1, 2023. The Alliance Funding Amount will be calculated annually at the conclusion of each payment period, and, to the extent the Company's annual aggregate payments to Moffitt of $3.5 million exceeds the applicable annual installment amount, the Company will receive a reduction in the amount due for future installment payments based on a predetermined formula agreed to by the parties. To the extent the aggregate annual payments are less than $3.5 million, the Company will prepay the remaining amount due.

In connection with the execution of the Alliance Agreement, the Company issued Moffitt 91,721 shares of its common stock. As partial consideration under the Alliance Agreement, the Company also agreed to issue Moffitt an additional 366,884 shares of its common stock in the aggregate upon the satisfaction of certain clinical and regulatory milestones with respect to TIL Products. The issuances of common stock are treated as performance-based stock awards. On February 27, 2023, 91,721 shares were issued due to the achievement of the milestone related to the start of the Phase 1 trial. In addition, upon achievement of certain thresholds for aggregate net sales of all TIL Products, the Company is required to make tiered sales-based milestones payments to Moffitt of up to an aggregate of $50.0 million. With respect to each of the equity and sales milestones described above, TIL Products include any pharmaceutical, biopharmaceutical or biotechnology TIL Product that is developed by the Company or Moffitt and is advanced into clinical development under an IND sponsored by Moffitt.

Unless earlier terminated, the Alliance Agreement will remain in effect for a term of five years and may be extended for additional periods upon the mutual written consent of both parties. Either party may terminate the Alliance Agreement in the event of (i) the other party's material breach of the Alliance Agreement that remains uncured after ninety days of receiving written notice of such breach (or in the case of breach of payment obligations, within ten days), (ii) the other party's insolvency and (iii) a pandemic event resulting in government lockdowns or orders that legally compel such party to cease operations or that result in material disruptions in the available workforce and prevents such party from performing its contractual obligations for a period of more than six months. At any time after June 1, 2025, either party may terminate the Alliance Agreement without cause upon sixty days prior written notice to the other party (a "Termination for Convenience"). Upon a Termination for Convenience, the terminating party shall pay to the other party a termination fee in an amount equal to a low double digit percentage of the then remaining Alliance Funding Amount. Termination or expiry of one or more Underlying Agreements does

not affect the term of the Alliance Agreement, which will continue to apply to the remaining ongoing Underlying Agreements.

7. Asset Acquisition

In December 2020, the Company entered into the Agreement and Plan of Merger and Reorganization (the "Myst Merger Agreement"), by and among the Company, Flatiron Merger Sub I, Inc. ("Merger Sub"), Flatiron Merger Sub II, LLC ("Merger LLC"), a direct, wholly-owned subsidiary of the Company, Myst Therapeutics, Inc. ("Myst"), and Timothy Langer, the sole common stockholder of Myst ("Langer"). Pursuant to the Myst Merger Agreement, the business combination (the "Merger") was affected in two steps. The first step was the merger of Merger Sub with and into Myst. The second step was the merger of Myst with and into Merger LLC. The Merger closed on December 14, 2020, and the effective date of the Merger was January 20, 2021. As a result of the Merger, the separate existences of Merger Sub and Myst ceased, and Merger LLC became the Company's wholly-owned subsidiary.

Pursuant to the Myst Merger Agreement, on December 15, 2020, the Company paid the former equity holders of Myst, (the "Myst Holders"), a one-time up-front payment of $9.0 million in cash. The Company paid an additional cash consideration of $1.0 million to the Myst Holders on June 14, 2022. The Company also issued Langer up to 725,920 shares of the Company's common stock. Of these shares, 362,960 shares of the Company's common stock were issued upon the closing of the Merger and the remaining 362,960 shares of the Company's common stock were held in escrow with 25% vesting in December of each year that Langer remains an employee of the Company. As of December 31, 2023, Langer is still employed by the Company and 272,220 shares of the Company's common stock have vested and been released from escrow with the remaining 90,740 shares of the Company's common stock to be released in December 2024, based on his continued employment. This restricted equity grant is accounted for as a compensatory arrangement under ASC 718 as continued service is required under the agreement. fo

In addition, under the Myst Merger Agreement, each Myst Holder is entitled to receive certain payments as consideration based on the achievement by the Company of three predefined milestones. The initial milestone is the closing of an initial public offering, which occurred on July 25, 2023, the second milestone is the first acceptance by the FDA of an IND filed by, on behalf of or for the benefit of the Company, or the Company's sublicensees for a product being developed by or on behalf of the Company or its sublicensees that is claimed as a product or method of making or using the product by a pending or issued Myst patent claim existing at the time of such acceptance, and the third milestone is the occurrence of the earlier of (i) the commencement of the first registration study for a product being developed by, on behalf of or for the benefit of the Company that is claimed as a product or a method of making or using the product by an issued Myst patent claim existing as of the time of such commencement or (ii) the issuance of a Myst patent claim that claims a product or method of making or using the product then being developed by, on behalf of or for the benefit of the Company, or its sublicensees, that is or was the subject of a registration study that has or had commenced. The milestones are not contingent on one another, and the milestones do not need to be achieved in any specific order.

Within 45 days of the achievement of the initial milestone, which occurred on July 25, 2023, the Company is obligated to pay the Myst Holders an aggregate amount equal to $3.0 million. At the Company's election, the Company may pay this consideration in cash or in shares of the Company's common stock. Pursuant to a letter agreement dated September 11, 2023 between the Company and the former equityholders of Myst regarding the $3.0 million milestone payment that became due and owing to the Myst Holders, the Company agreed to pay $0.2 million in cash to the former optionholders of Myst on or before September 30, 2023, with the remaining $2.8 million payable to Langer in shares of the Company's common stock. On September 11, 2023, the Company issued 249,992 shares of the Company's common stock to Langer.

Within 45 days of the achievement of the second milestone, the Company is obligated to pay the Myst Holders an aggregate amount equal to $10.0 million. At the Company's election, the Company may pay this consideration in cash or in shares of the Company's common stock. In May 2022, this $10.0 million milestone was achieved. The Company elected to pay $5.0 million in the Company's common stock and $5.0 million in cash. Pursuant to a letter agreement dated July 25, 2022 between the Company and the former equityholders of Myst regarding the $10.0 million milestone payment that became due and owing to the Myst Holders, the Company

agreed to pay to the former optionholders of Myst on or before July 28, 2022, $0.6 million in cash, with the remaining $9.4 million payable to Langer as follows: (i) on or before July 28, 2022, $2.2 million in cash, (ii) on or before July 31, 2022, $5.0 million in shares of the Company's common stock and (iii) on or before January 10, 2023, $2.2 million in cash. On June 8, 2022, the Company issued Langer 212,203 shares of the Company's common stock to settle the $5.0 million obligation payable in common stock. The Company then paid the Myst Holders $2.8 million in July 2022, with $2.2 million paid to Langer and $0.6 million paid to the remaining Myst Holders, and the remaining $2.2 million was paid to Langer in January 2023.

Within 45 days of the achievement of the third milestone, the Company is obligated to pay the Myst Holders an aggregate amount equal to $20.0 million. At the Company's election, the Company may pay this consideration in cash or in shares of its common stock.

The Company accounted for the merger with Myst pursuant to the Myst Merger Agreement as an asset acquisition as substantially all of the value received was concentrated in the acquired in-process research and development of Myst and did not have an alternate future use. The Company recognized a $19.4 million charge to research and development expense at the time of the completion of the asset acquisition during the year ended December 31, 2020. The Company determined that the milestone payments are separate units of account and accounted for the initial milestone as a derivative in accordance with ASC 815 and the second and third milestones as liabilities in accordance with ASC 480. In connection with the initial public offering, the Company reassessed its initial accounting of the milestone payments and concluded that they should be viewed as one unit of account because the milestone payments are not legally detachable from each other. The milestone payments, as one unit of account, would be classified as a liability in accordance with ASC 480 and measured at fair value, with changes in the fair value recorded in earnings. Regardless of whether the milestone payments are viewed as one unit of account or three units of account, because they are all subject to fair value measurement, the financial reporting effect of the contingent consideration arrangement as one unit of account or three units of account is substantially the same. As a liability under ASC 480, the contingent consideration will continue to be recorded at fair value until settled. The adjustment to the fair value of the contingent consideration of $0.9 million and $7.0 million for the twelve months ended December 31, 2023 and 2022, respectively were included in research and development expense in the Company's consolidated statements of operations and comprehensive loss.

8. Redeemable Convertible Preferred Stock and Stockholders' Equity

Redeemable Convertible Preferred Stock

From October 2015 to October 2016, the Company issued a total of 11,250,000 shares of series A preferred stock (the "Series A Preferred Stock") at CDN$1.00 per share (equivalent to $0.74 per share, based on a conversion ratio of 1.344 Canadian dollars to one U.S. dollar) for total net proceeds of CDN$ 10.9 million (equivalent to $8.1 million based on a conversion ratio of 1.344 Canadian dollars to one U.S. dollar).

In October 2016, the Company issued a total of 16,285,156 shares of series B-1 preferred stock (the "Series B-1 Preferred Stock") at $0.77 per share for total net proceeds of $12.3 million. In November 2018, the Company issued 25,065,538 shares of series B-2 preferred stock (the "Series B-2 Preferred Stock", and together with the Series B-1 Preferred Stock, the "Series B Preferred Stock") at $1.15 per share for total net proceeds of $28.9 million.

The Company issued a total of 17,905,288 shares of series C preferred stock (the "Series C Preferred Stock") at $2.35 per share in January 2019 for net proceeds of $41.8 million.

The Company issued a total of 29,285,356 shares of series D preferred stock (the "Series D Preferred Stock") at $2.73 per share in June 2021 for net proceeds of $79.8 million.

In connection with the Company's IPO, all outstanding shares of the Company's redeemable convertible preferred stock automatically converted into 12,493,879 shares of common stock. Subsequent to the closing of the IPO, there were no shares of redeemable convertible preferred stock outstanding.

Common Stock

In connection with the closing of the IPO, the Company filed its Amended and Restated Certificate of Incorporation which provides that the authorized common stock of the Company is 490,000,000 shares of common stock with a par value of $0.001 per share. Holders of outstanding shares of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the holders of common stock. Subject to the rights of the holders of any class of the Company's capital stock having any preference or priority over common stock, the holders of common stock are entitled to receive dividends that are declared by the Company's board of directors out of legally available funds. In the event of a liquidation, dissolution or winding-up, the holders of common stock are entitled to share ratably in the net assets remaining after payment of liabilities, subject to prior rights of preferred stock, if any, then outstanding. The common stock has no preemptive rights, conversion rights, redemption rights or sinking fund provisions, and there are no dividends in arrears or default. All shares of common stock have equal distribution, liquidation and voting rights, and have no preferences or exchange rights.

Shares of common stock reserved for future issuance, on an as-if-converted basis, consisted of the following:

	December 31, 2023	December 31, 2022
Series A redeemable convertible preferred stock	—	1,408,502
Series B-1 redeemable convertible preferred stock	—	2,038,903
Series B-2 redeemable convertible preferred stock	—	3,138,208
Series C redeemable convertible preferred stock	—	2,241,740
Series D redeemable convertible preferred stock	—	3,666,526
Common stock options outstanding	3,374,282	2,529,982
Unvested RSUs	102,945	—
Shares available for issuance under the ESPP	222,287	—
Shares available for issuance under the Plans	1,755,404	255,685
	5,454,918	15,279,546

9. Equity Based Compensation

2018 Equity Incentive Plan

In December 2018, the Company adopted the 2018 Equity Incentive Plan (the "2018 Plan") which provided for the Company to grant incentive stock options or nonqualified stock options for the purchase of common stock, or restricted shares, to employees, members of the board of directors and consultants of the Company. The Company assumed all of the outstanding options under the amended and restated Equity Incentive Plan of Turnstone Biologics Inc. dated October 1, 2016 (the "2016 Plan") in connection with the corporate reorganization in December 2018. However, there were no changes to the terms of the options requiring modification accounting.

All options granted under the 2018 Plan have an exercise price, a vesting period determine by the Company's board of directors and ten-year term as determined and approved by the Company's board of directors (the board of directors may delegate authority to one of the boards' committees) at the time of grant. The terms and conditions of the restricted shares are determined by the board of directors at the grant date.

The majority of grants outstanding were approved with a four-year vesting schedule with 25% vesting after one year and the remainder vesting evenly over the remaining 36 months. Upon the effectiveness of the 2023 Plan defined and described below, no further grants will be made under the 2018 Plan. Any outstanding awards granted under these plans will remain subject to the terms of their 2016 and 2018 Plans, respectively, and applicable award agreements.

2023 Equity Incentive Plan

In July 2023, the Company's board of directors and stockholders adopted the 2023 Equity Incentive Plan (the "2023 Plan" and together with the 2018 and 2016 Plans the "Plans") which became effective upon the date of the IPO. Under the 2023 Plan, the Company may grant stock options, stock appreciation rights, restricted stock, RSUs,

performance stock awards, performance cash awards and other forms of stock awards to employees, directors and consultants. The maximum term of the stock option grants under the 2023 Plan is ten years. In general, the awards granted under the 2023 Plan vest over a four-year period from the vesting commencement date. The 2023 Plan does not permit early exercises. The number of shares available for future issuance under the 2023 Plan is the sum of (1) 1,889,435 new shares, plus (2) 712,503 remaining shares of common stock reserved under the 2018 Plan that became available for issuance upon the effectiveness of the 2023 Plan, and (3) up to 120,949 Returning Shares (as defined in the 2023 Plan), as such shares become available from time to time. The number of shares of common stock reserved for issuance under the 2023 Plan will automatically increase on January 1 of each year, for a period of ten years, from January 1, 2024 continuing through January 1, 2033, by 5% of the total number of shares of common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by the Company's board of directors. There was no limitation for 2024. Following the effectiveness of the 2023 Plan, no further grants may be made under the 2018 Plan; however, any outstanding equity awards granted under the 2018 Plan will continue to be governed by the terms of the Plan.

A summary of the stock option activity under the Plans is as follows:

	Number of Shares Underlying Outstanding Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding — December 31, 2021	1,759,275	$ 7.26	7.2	$ 6,912
Options granted	951,543	$ 11.02		
Options exercised	(61,355)	$ 2.55		
Options canceled/forfeited	(119,481)	$ 5.75		
Outstanding — December 31, 2022	2,529,982	$ 8.86	6.8	$ 5,886
Options granted	1,028,355	$ 5.44		
Options exercised	(29,715)	$ 3.49		
Options canceled/forfeited	(154,340)	$ 10.29		
Outstanding — December 31, 2023	3,374,282	$ 7.66	7.1	$ 352
Exercisable — December 31, 2023	1,792,591	$ 7.93	5.3	$ 347
Vested and expected to vest — December 31, 2023	3,374,282	$ 7.66	7.1	$ 352

The fair value of each stock option granted to employees and directors was estimated on the date of grant using the Black-Scholes option-pricing model, with the following range of assumptions:

	Year Ended December 31,	
	2023	2022
Risk-free interest rate	3.9% - 4.8%	1.7% - 3.6%
Expected term (in years)	5.8 - 6.2	5.7 - 6.0
Dividend yield	0.0%	0.0%
Volatility	85.8% - 88.2%	86.3% - 87.2%
Weighted-average exercise price of stock options granted	$5.44	$11.02

As of December 2023, the Company grants RSUs to employees. The RSU activity is summarized as follows:

	Number of RSUs	Weighted-Average Grant Date Fair Value
Outstanding, non-vested as of December 31, 2022	—	$ —
Granted	102,945	$ 2.71
Cancelled/Forfeited	—	—
Vested/Released	—	—
Outstanding, non-vested as of December 31, 2023	102,945	$ 2.71

The allocation of stock-based compensation expense for all stock awards, including options, restricted stock and RSUs, included in the Company's statements of operations is as follows (*in thousands*):

	Year Ended December 31,	
	2023	2022
Research and development	$ 2,274	$ 2,167
General and administrative	1,942	2,201
Total stock-based compensation	$ 4,216	$ 4,368

The weighted-average grant date Black Scholes fair market value of options granted to employees, directors and consultants during the twelve months ended December 31, 2023 and 2022 was $4.06 per share and $7.91 per share, respectively. The total weighted-average grant date fair value of RSUs granted by the Company during the year ended December 31, 2023 was $0.3 million.

As of December 31, 2023, the Company had unrecognized stock-based compensation expense of $7.0 million and $0.3 million, related to stock options and RSUs respectively, which is expected to be recognized over a weighted-average period of 3.0 years and 3.9 years, respectively.

Restricted Stock

In December 2020, Langer received 725,920 shares as payment related to the Myst Merger Agreement. Of the total issued, the Company restricted 362,960 shares to vest over a four-year period in equal annual installments. As of December 31, 2023, 90,740 shares remain unvested, and the Company had $0.9 million in unrecognized stock-based compensation expense related to unvested restricted stock which is expected to be recognized evenly over 1 year.

2023 Employee Stock Purchase Plan

In July 2023, the Company adopted the Employee Stock Purchase Plan (the "ESPP"), which became effective with the IPO on July 25, 2023. The ESPP was adopted by the Company's board of directors and stockholders in June 2023. The ESPP initially provides participating employees with the opportunity to purchase up to an aggregate of 222,287 shares of common stock. The number of shares of common stock reserved for issuance will automatically increase on January 1st of each calendar year for a period of up to ten years, commencing on January 1, 2024 and ending on (and including) January 1, 2033, in an amount equal to the lesser of (i) one percent (1%) of the total number of shares of capital stock outstanding on the last day of the calendar month before the date of the automatic increase, and (ii) 666,680 shares of common stock. Notwithstanding the foregoing, the board may act prior to the first day of any calendar year to provide that there will be no January 1st increase in the share reserve for such calendar year or that the increase in the share reserve for such calendar year will be a lesser number of shares of common stock than would otherwise occur pursuant to the preceding sentence. There was no limitation for 2024. As of December 31, 2023, there was no enrollment offered to the Company's employees.

10. Income Taxes

The following table represents the components of net loss before income taxes (*in thousands*):

	Year Ended December 31,	
	2023	2022
Domestic	$ (52,765)	$ (22,065)
Foreign	(2,721)	(8,628)
Loss before provision for income taxes	$ (55,486)	$ (30,693)

The income tax provision consisted of the following (*in thousands*):

	Year Ended December 31,	
	2023	2022
Current:		
Federal	$ (522)	$ 80
State taxes	236	61
Deferred:		
Federal		—
State		—
Total tax provision (benefit)	$ (286)	$ 141

The reconciliation of the expected provision for income tax recovery to the actual provision for income tax expense reported is as follows *(in thousands)*:

	Year Ended December 31,	
	2023	2022
Loss before income taxes	$(55,486)	$(30,693)
Statutory rate	21%	21%
Expected income tax recovery	(11,652)	(6,446)
Permanent differences	211	260
Foreign rate differential	(149)	(462)
Canada ITC credits	(715)	(1,617)
Federal R&D credit	(1,776)	(1,637)
Unrecognized tax benefit	(13)	22
State tax	3,348	(2,422)
Myst transaction	210	1,877
Other	1,337	(4)
Change in valuation allowance	9,525	10,570
R&D credit carryback claim	(612)	—
Provision for income taxes (benefit) expenses	$ (286)	$ 141

The significant components of the Company's deferred income tax assets are as follows (*in thousands*):

	Year Ended December 31,	
	2023	2022
Deferred tax assets:		
Credits	$ 10,874	$ 7,960
Accruals	125	108
Stock compensation	898	1,111
State taxes	1	33
Right-of-use lease liability	680	1,319
Property and equipment	—	144
Intangibles	20,726	16,858
Tax losses	14,783	7,253
Deferred revenue	—	5,290
Total deferred tax assets	$ 48,087	$ 40,076
Deferred tax liability:		
Right-of-use lease asset	$ (588)	$ (1,174)
Property and equipment	(734)	(1,665)
Unrealized gains/losses	(3)	—
Total deferred tax liability	$ (1,325)	$ (2,839)
Valuation allowance	(46,762)	(37,237)
Net deferred tax assets	$ 0	$ 0

As of December 31, 2023, the Company had approximately $39.7 million of U.S. federal and $9.3 million of state net operating loss, or NOL, carryforwards. The Company's U.S. federal NOL carryforwards can be carried forward indefinitely, but use of such carryforwards is limited to 80% of taxable income. If not utilized, the Company's state NOL carryforwards will begin to expire at various dates beginning in 2038.

Furthermore, under Section 382 of the Internal Revenue Code of 1986, the amount of benefits from the Company's NOL carryforwards may be impaired or limited if we incur a cumulative ownership change of more than 50% over a three-year period. The Company has not conducted an analysis as to whether such a change of ownership has occurred, but if such a change has occurred or occurs in the future, the Company will be limited regarding the amount of NOL carryforwards that can be utilized annually in the future to offset taxable income. Any such annual limitation may significantly reduce the value of the Company's NOL carryforwards before they expire, which could result in greater tax liabilities than the Company would incur in the absence of such a limitation.

The Company has determined that it is not more likely than not that it will realize all of its deferred tax assets, and therefore a valuation allowance has been established against the deferred tax assets for Canadian and U.S. State jurisdictions. The Company files federal and provincial income tax returns in Canada and federal, state and local U.S. Income tax returns.

For the Canadian Entity the Company estimates SR&ED expenditures and claims investment tax credits for income tax purposes based on management's interpretation of the applicable legislation in the Income Tax Act (the "Act") and related provincial legislation. These claims are subject to audit by the tax authorities. In the opinion of management, the treatment of research and development expenditures for income tax purposes is appropriate. Any difference between recorded refundable tax credits and amounts ultimately received is recorded when the amount becomes known.

In the ordinary course of its business for the U.S. entity, the Company incurs costs that, for tax purposes, are determined to be qualified research expenditures within the meaning of IRC §41 and are, therefore, eligible for the Increasing Research Activities credit under IRC §41. The federal Research and Development credit ("R&D Credit") carryforward as of December 31, 2023 is $5.0 million that will expire in 2039, and the California R&D credit carryforward of $2.3 million as of December 31, 2023 has no expiration date.

As of December 31, 2023, the Company has total uncertain tax benefits of $2.2 million related to the R&D credit, of which $1.9 million is recorded as a reduction of the deferred tax asset related credit carryforward. If the uncertain tax benefits were to be recognized, there would be an impact to the effective tax rate. No interest or penalties have been recorded related to the uncertain tax positions. However, the impact would be immaterial. The Company's policy is to include interest and penalties related to uncertain tax benefits as other expense.

The aggregate changes in the balances of the Company's gross unrecognized tax benefits during 2023 were as follows (*in thousands*):

December 31, 2022	$	(857)
Increases in balances related to tax positions taken during a prior period		(541)
Increases in balances related to tax positions taken during the current period		(799)
Decreases in balances related to tax positions tax during the prior period		—
December 31, 2023	$	(2,197)

It is not expected that there will be a significant change in uncertain tax position in the next 12 months.

The Company is subject to U.S. federal and state income tax as well as to income tax in multiple state jurisdictions. In the normal course of business, the Company is subject to examination by tax authorities. As of the date of the consolidated financial statements, there are no tax examinations in progress. The statute of limitations for tax years ended after December 31, 2020 are open for state and federal tax purposes.

At December 31, 2023, the Canadian Entity had carryforward balances which are available to offset future years' taxable income. At December 31, 2023, the Company had non-refundable investment tax credits amounting to $7.6 million that begin to expire in 2038 and an SR&ED expenditure pool of $21.9 million that does not expire. During 2023, the Company expects to utilize $0.0 million of non-capital losses and $0.5 million of investment tax credits to offset its 2023 Canada tax liability.

On June 29, 2020, the California governor signed Assembly Bill 85 ("A.B. 85"), which includes several tax measures to close a gap in the budget created by the COVID-19 pandemic. The most significant provisions of the bill are (i) the suspension of taxpayers' ability to deduct net operating losses during tax years 2020, 2021, and 2022; and (ii) the limitation on the amount of tax that can be offset by business credits to $5 million for tax years 2020, 2021, and 2022. For corporate taxpayers, if their income subject to California taxation is less than $1.0 million the suspension does not apply. On February 9, 2022, the California Governor signed Senate Bill 113 "SB 113". SB 113 which removes the suspension of NOL and the limitation on the amount of tax that can be offset by business credits to $5.0 million provisions included in A.B. 85 for the 2022 tax year. Thus, the Company is not expecting its net operating loss carryover to be limited for the tax year ending December 31, 2022.

11. Leases

Operating Leases

The Company leases laboratory and office space for its corporate headquarters located in San Diego, California as well as in New York, New York and Ontario, Canada. Operating lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term. In calculating the present value of the lease payments, the Company has elected to utilize its incremental borrowing rate based on the original lease term and not the remaining lease term. The Company determines if an arrangement is a lease by considering whether there is an identified asset, and the contract conveys the right to control its use. Leases with an initial term of 12 months or less are not recorded on the balance sheet. The Company's lease terms may include options to extend or terminate a lease. If the lease includes non-lease components (i.e., common area maintenance) that are paid separately from rent based on actual costs incurred and therefore are not included in the right-of-use asset and lease liability but are reflected as an expense in the period incurred.

In July 2018, the Company entered into a lease agreement for approximately 6,500 square feet of office space in New York, New York. The term of the lease is seven years and three months, starting November 1, 2018. The lease requires the Company to share in prorated expenses and property taxes based upon actual amounts incurred. The lease contains escalating rent clauses which require higher rent payments in future years. In September 2022, the Company made the decision to sublease this space and executed a sublease in November 2022 for the remaining term of the lease. Since the Company is still responsible for making the lease payments, there was no impact to the operating lease liability from the sublease. However, since the sublease payment does not cover the entire lease payment, the carrying value of the operating right of use asset was analyzed and determined to be impaired resulting in a $0.5 million reduction in the operating right of use asset in September 2022.

In January 2019, the Company executed an agreement to lease approximately 6,000 square feet of laboratory space at Carleton University in Ontario, Canada. The initial term of the lease is three years and started in November 2019 at a rate of approximately $0.1 million per year. In November 2022, the lease was extended for a one year period. In August 2023, the Company terminated the lease.

In May 2019, the Company entered into a noncancelable operating lease for approximately 9,423 square feet located at 12 York Street, Ontario, CA. The term of the lease is five years, starting December 1, 2019, and includes one renewal option for a period of five years. The lease requires the Company to share in prorated expenses and property taxes based upon actual amounts incurred. The lease contains escalating rent clauses which require higher rent payments in future years.

In June 2021, the Company entered into a lease agreement for approximately 19,474 square feet of office and laboratory space in San Diego, California. The initial term of the lease is 38 months with one renewal option for a period of three years and commenced in March 2022. The lease requires the Company to share in prorated expenses and property taxes based upon actual amounts incurred. The lease contains escalating rent clauses which require higher rent payments in future years.

The Company recorded rent expense of $1.6 million and $2.3 million for the twelve months ended December 31, 2023 and 2022, respectively. The table below summarizes the Company's total lease costs included in its consolidated financial statements, as well as other required quantitative disclosures (*in thousands*).

	Year Ended December 31,	
	2023	2022
Operating lease cost	$ 2,074	$ 1,956
Short-term lease costs	4	263
Variable leases costs	5	52
Sublease income	(477)	(21)
Total lease cost	$ 1,606	$ 2,250

The present value assumptions used in calculating the present value of the lease payments were as follows:

	Year ended December 31, 2023
Weighted-average remaining lease term in years	1.7
Weighted-average discount rate	5.0%

The minimum aggregate future operating lease commitments at December 31, 2023 are as follows (*in thousands*):

	Minimum Lease Payments
2024	2,133
2025	1,110
2026	104
2027	—
2028	—
Total undiscounted lease payments	$ 3,347
Less: imputed interest	(133)
Total operating lease liability	3,214
Less: current portion of operating lease liability	(2,025)
Operating lease liability, noncurrent	$ 1,189

12. 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, 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 anti-dilutive. Potentially dilutive common shares have been excluded from the diluted net loss per common share computations in all periods presented because such securities have an anti-dilutive effect on net loss per common share due to the Company's net loss. There are no reconciling items used to calculate the weighted-average number of total common shares outstanding for basic and diluted net loss per common share.

The following outstanding potentially dilutive shares were excluded from the computation of diluted net loss per share attributable to common stockholders:

	Year Ended December 31,	
	2023	2022
Redeemable convertible preferred stock	—	12,493,879
Restricted stock	90,740	181,480
Unvested RSUs	102,945	—
Options to purchase common stock	3,374,282	2,529,982
Total	3,567,967	15,205,341

13. Legal Proceedings

The Company is not a party to any material legal matters or claims and does not have contingency reserves established for any litigation liabilities as of the years ended December 31, 2023 and 2022, respectively.

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, 2023, management, with the participation and supervision of our Chief Executive Officer and our Chief Financial Officer, have evaluated our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Based on that evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that, as of December 31, 2023, our disclosure controls and procedures were effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Changes in Internal Control over Financial Reporting

Due to a transition period established by SEC rules applicable to newly public companies, our management is not required to evaluate the effectiveness of our internal control over financial reporting until after the filing of our Annual Report on Form 10-K for the year ended December 31, 2023.

Item 9B. Other Information.

Not applicable.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item and not set forth below will be set forth in our definitive Proxy Statement to be filed with the Commission within 120 days after the conclusion of our year ended December 31, 2023 (the "Proxy Statement") pursuant to General Instructions G(3) of Form 10-K and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or person performing similar functions. A current copy of the Code of Business Conduct and Ethics is available on the Corporate Governance section of our website at www.ir.turnstonebio.com. If we make any substantive amendments to the Code of Business Conduct and Ethics or grants any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director that are required to be disclosed pursuant to SEC rules, we will promptly disclose the nature of the amendment or waiver on our website or in a current report on Form 8-K.

Item 11. Executive Compensation.

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

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

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

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

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) Documents filed as part of this report.

(1) Financial Statements. The following financial statements of Turnstone Biologics Corp., together with the report of Ernst & Young LLP, an independent registered public accounting firm required to be filed pursuant to Part II, Item 8 of the Annual Report on Form 10-K are included on the following pages:

EXHIBITS INDEX

Exhibit No.	Description	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
2.1	Agreement and Plan of Merger and Reorganization, dated December 11, 2020, between Turnstone Biologics Corp., Flatiron Merger Sub I, Inc., Flatiron Merger Sub II, LLC, Myst Therapeutics, Inc. and Timothy Langer.	S-1/A	333-272600	2.1	July 17, 2023
3.1	Amended and Restated Certificate of Incorporation of the Company.	8-K	001-41747	3.1	July 25, 2023
3.2	Amended and Restated Bylaws of the Company.	8-K	001-41747	3.2	July 25, 2023
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-272600	4.1	June 26, 2023
4.2	Second Amended and Restated Investors' Rights Agreement, by and among Turnstone Biologics Corp. and certain of its stockholders, dated June 29, 2021	S-1	333-272600	4.2	June 12, 2023
4.3*	Description of Securities		333-272600		
10.1	Amended and Restated Equity Incentive Plan and Forms of Option Agreement and Exercise Notice thereunder	S-1	333-272600	10.1	June 12, 2023
10.2	2018 Equity Incentive Plan and Forms of Option Agreement and Exercise Notice thereunder	S-1	333-272600	10.2	June 12, 2023
10.3	2023 Equity Incentive Plan and Forms of Option Agreement and Exercise Notice thereunder	S-1/A	333-272600	10.3	July 17, 2023
10.4	Turnstone Biologics Corp. 2023 Employee Stock Purchase Plan	S-1/A	333-272600	10.4	July 17, 2023
10.5	Turnstone Biologics Corp. 2023 Non-Employee Director Compensation Policy	S-1/A	333-272600	10.5	July 17, 2023
10.6	Form of Indemnity Agreement between Turnstone Biologics Corp. and each of its directors and executive officers	S-1/A	333-272600	10.6	June 26, 2023
10.7#	Amended and Restated Master Collaboration Agreement, dated January 1, 2021, between Turnstone Biologics Corp. and H. Lee Moffitt Cancer Center and Research Institute, Inc.	S-1	333-272600	10.7	June 12, 2023

Exhibit No.	Description	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
10.8#	Life Science Alliance Agreement, dated June 1, 2022, by and between H. Lee Moffitt Cancer Center and Research Institute, Inc. and Turnstone Biologics Corp.	S-1	333-272600	10.8	June 12, 2023
10.9	Lease, dated June 23, 2021, between Turnstone Biologics Corp. and BMR-Athena LP	S-1	333-272600	10.9	June 12, 2023
10.10	Employment Offer Letter, dated August 20, 2015, between Turnstone Biologics Inc. and Sammy Farah, M.B.A., Ph.D.	S-1	333-272600	10.10	June 12, 2023
10.11	Employment Offer Letter, dated December 13, 2021, between Turnstone Biologics Corp. and Venkat Ramanan, Ph.D.	S-1	333-272600	10.11	June 12, 2023
10.12	Employment Offer Letter, dated May 7, 2021, between Turnstone Biologics Corp. and Stewart Abbot, Ph.D.	S-1	333-272600	10.12	June 12, 2023
10.13	Employment Offer Letter, dated September 18, 2019, between Turnstone Biologics Inc. and Saryah Azmat	S-1	333-272600	10.13	June 12, 2023
10.14	Executive Director Offer Letter, dated April 30, 2021, between Turnstone Biologics Corp. and Michael Burgess, MBChB, Ph.D.	S-1	333-272600	10.14	June 12, 2023
10.15	Employment Offer Letter, dated February 22, 2022, between Turnstone Biologics Corp. and Michael Burgess, MBChB, Ph.D.	S-1	333-272600	10.15	June 12, 2023
10.16	Employment Offer Letter, dated March 1, 2023, between Turnstone Biologics Corp. and Vijay Chiruvolu, Ph.D.	S-1	333-272600	10.16	June 12, 2023
21.1	Subsidiaries of Turnstone Biologics Corp.	S-1	333-272600	21.1	June 12, 2023
23,1*	Consent of Independent Registered Public Accounting Firm				
24.1*	Power of Attorney (see signature page)				
31.1*	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
31.2*	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
32.1*+	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
97.1	Turnstone Biologics Corp. Incentive Compensation Recoupment Policy				
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.				
101.SCH*	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents				
104*	Cover Page Interactive Data File (embedded within the Inline XBRL document)				

* Filed herewith.
+ Furnished herewith and not deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of La Jolla, State of California, on the X day of March, 2024.

Turnstone Biologics Corp.

Date: March 21, 2024

By: */s/ Venkat Ramanan*

Venkat Ramanan, Ph.D.
Chief Financial Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Sammy Farah, M.B.A., Ph.D., and Venkat Ramanan, Ph.D., and each of them, as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her and in his or her name, place or 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 and about the premises, 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 their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ *Sammy Farah* **Sammy Farah, M.B.A., Ph.D.**	President, Chief Executive Officer, Director	March 21, 2024
/s/ Venkat Ramanan Venkat Ramanan, Ph.D.	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 21, 2024
/s/ Michael Burgess Michael Burgess, MBChB, Ph.D.	Interim Chief Medical Officer and Director	March 21, 2024
/s/ Jerel Davis Jerel Davis, Ph.D	Director	March 21, 2024
/s/Robert Gould Robert Gould, Ph.D.	Director	March 21, 2024
/s/ Rishi Gupta Rishi Gupta	Director	March 21, 2024
/s/ Patrick Machado Patrick Machado	Director	March 21, 2024
/s/ Kanya Rajangam Kanya Rajangam, Ph.D	Director	March 21, 2024