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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2022
OR

☐ **TRANSITION REPORT UNDER SECTION 13 OR 15(d) OF THE EXCHANGE ACT**

Sigilon Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-39746**	**47-4005543**
(State or other jurisdiction of incorporation or organization)	(Commission File No.)	(I.R.S. Employer Identification No.)

100 Binney Street, Suite 600
Cambridge, MA 02142
(Address, including zip code, of registrant's principal executive offices)

(617) 336-7540
(Registrant's telephone number, including area code)

Securities Registered Pursuant to Section 12(b) of the Act:

Title of Each Class	**Trading Symbol(s)**	**Name of Each Exchange on Which Registered**
Common Stock, $0.001 par value per share	SGTX	The Nasdaq Global Select Market

Securities Registered Pursuant to Section 12(g) of the Act: None

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

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

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

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

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

Large accelerated filer ☐	Accelerated filer ☐	Non-accelerated filer ☒	Smaller reporting company ☒
			Emerging growth company ☒

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

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

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

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

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

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant as of June 30, 2022 was approximately $18,238,725, computed by reference to the closing price of the registrant's common stock on the Nasdaq Global Select Market reported for such date.

As of March 1, 2023, there were 32,466,737 shares of common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the registrant's definitive proxy statement that will be filed for the 2022 Annual Meeting of Stockholders are incorporated by reference in Part III.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, forward-looking statements include terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements concerning:

- the timing and progress of our research and development programs and preclinical studies and the submission or approval of Investigational New Drug, or IND, applications for our product candidates, including our plans to conduct non-human primate and IND-enabling studies for SIG-002 in the second half of 2023, with an expected IND submission in 2024;

- our ability to advance any product candidates that we may develop and successfully complete any clinical studies, including the process development, scale up and manufacturing activities for our product candidates;

- our ability to fund our operating expenses, capital expenditures requirements and debt service payments into 2025;

- our belief that, at commercial scale, the cost of goods for some of our programs will be significantly lower than existing cell or gene therapies;

- our ability to identify and enter into future license agreements and collaborations; and

- estimates of our expenses, capital requirements and needs for additional financing.

There may be events in the future that we are not able to accurately predict or control and that may cause our actual results to differ materially from the expectations we describe in our forward-looking statements. We undertake no obligation to publicly update any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report on Form 10-K. We cannot guarantee future results, levels of activity, performance or achievements.

RISK FACTORS SUMMARY

Our business is subject to a number of risks, including risks that may adversely affect our business, results of operations, cash flows, and prospects. These risks are discussed more fully in "Item 1.A Risk Factors" and include, but are not limited to, risks related to:

- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- If we fail to achieve the expected financial and operational benefits of our corporate restructuring, our business and financial results may be harmed.
- If we cannot comply with Nasdaq's continued listing standards, our common stock could be delisted.
- Negative results of preclinical or clinical studies of any of our product candidates may require us to discontinue or delay development of other product candidates, which are all based on the same SLTx platform.
- The SLTx platform consists of novel technologies that are not yet clinically validated for human therapeutic use. The approaches we are taking to discover and develop novel therapeutics are unproven and may never lead to marketable products.
- We may not be successful in our efforts to identify and develop product candidates. If these efforts are unsuccessful, we may never become a commercial stage company or generate any revenues.
- We are early in our development efforts. It will be many years before we or our collaborators commercialize a product candidate, if ever.
- Drug development is a lengthy, expensive, and inherently uncertain process, with a high risk of failure at every stage of development, and any favorable preclinical results are not predictive of results that may be observed in future clinical trials.
- Our product candidates are composed of engineered human cell lines, encapsulated in a biocompatible matrix sphere. To date, there have been no completed human clinical trials for product candidates arising from our SLTx platform or consisting of our cell or sphere technologies. There may be serious adverse events, undesirable side effects related to either component of our product candidates, or limited efficacy of product candidates arising from our SLTx platform.
- If clinical trials of our current and future product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.
- If we are unable to obtain and maintain patent and other intellectual property protection for our product candidates and for our SLTx platform, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, our SLTx platform may be adversely affected.

PART I

Item 1. BUSINESS

As used in this Annual Report on Form 10-K, except as otherwise indicated by context, references to "we," "us," "our," "SGTX" or the "Company" refer to Sigilon Therapeutics Inc.

Overview

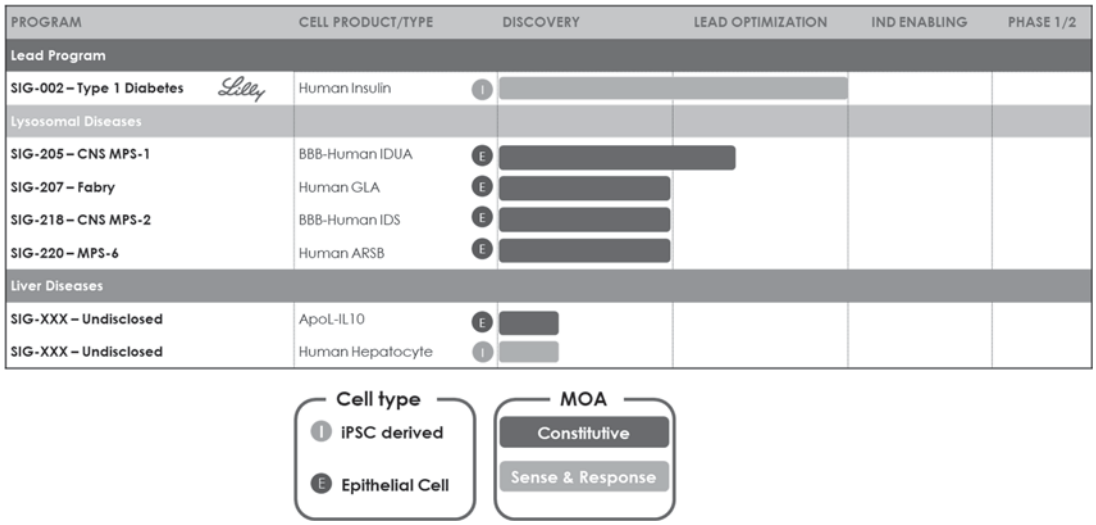
We are a preclinical stage biotechnology company pioneering a new class of therapeutics and seeking to develop functional cures for patients with acute and chronic diseases by providing stable and durable levels of therapeutic molecules to patients. Our Shielded Living Therapeutics, or SLTx, platform, which combines advanced cell engineering with cutting-edge innovations in cell differentiation and biocompatible materials, is designed to enable our product candidates to provide a wide range of functions or therapeutic molecules that may be missing or dysfunctional in patients. We are designing our product candidates to be off-the-shelf, durable, controllable and redosable, without requiring modification of the patient's genes or chronic suppression of the patient's immune system.

Our SLTx platform is comprised of two primary elements: the cells and the sphere. We differentiate stem cells into the appropriate cell types, such as islet cells in the case of our diabetes program, which both sense and respond. We also engineer cells to express a therapeutic molecule of choice in a continuous manner, which we refer to as constitutive expression. Our human cell lines are selected for each indication based on their safety, durability, scalability, functionality and engineerability. These cells are subsequently encapsulated in our proprietary and biocompatible spheres. The spheres are composed of an Afibromer outer layer, an alginate conjugated with a novel, proprietary small molecule, which was derived from 10 years of work in the MIT labs of Professors Robert Langer and Daniel Anderson. This work culminated in a series of patents and patent applications to which we obtained exclusive rights through our license agreement with MIT. The spheres are designed to prevent the generation of an immune response against the spheres encapsulating the cells while enabling nutrient influx and therapeutic protein efflux.

Modularity, a key attribute of our SLTx platform, is comprised of three core pillars: the cells, the sphere and the manufacturing process. In addition to the cells and the sphere described above, we have also spent significant time and resources to create a state-of-the-art modular manufacturing platform for all potential product candidates developed using our cell and sphere components. This cost-effective manufacturing platform is designed to provide a true "off-the-shelf" product for patients. Furthermore, virtually all aspects of the platform for a specific cell line, from raw materials to processing steps, can be shared across our development programs using such cell line, enabling a potentially streamlined path from discovery to clinical trials. This modularity has created an efficient engine for generation of product candidates.

Our Product Candidates and Platform Technology

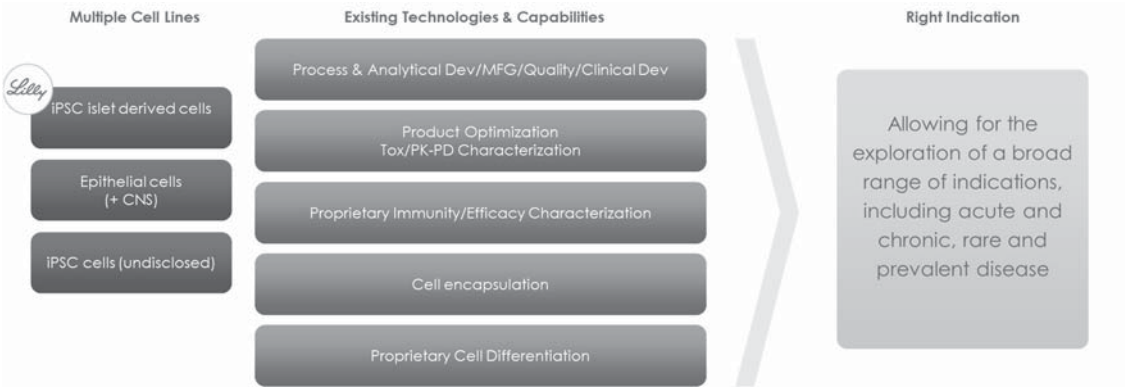
Leveraging the modularity of our platform and our scientific and preclinical work to date, we are able to advance programs in distinct therapeutic areas, including metabolic and other acute and chronic disorders. We are applying a strategic sequencing to the development of our portfolio, focusing on the potential to provide meaningful clinical benefit to patients, rapid time to proof of concept, clear regulatory path, and validated biology and clinical endpoints. Our current pipeline of SLTx product candidates is summarized in the figure below.



SIG-002, our lead product candidate, is designed to replace islet cells for the treatment of Type 1 Diabetes, or T1D. In T1D, the immune system attacks and destroys the insulin producing beta cells within the endocrine islets of the pancreas. Insulin deficiency results in dysregulation of glucose metabolism. In April 2018, we partnered with Eli Lilly and Company, or Lilly, to develop cell therapies for the treatment of T1D, including SIG-002. Under the terms of the partnership, we are currently leading execution of the program through IND submission and Lilly, a global leader in diabetes, will develop and commercialize the program worldwide. We expect to conduct IND-enabling activities for SIG-002 in 2023, with an expected IND submission in 2024. We received an upfront payment of $62.5 million as well as a $13.1 million equity investment from Lilly. We are eligible to receive up to $165.0 million in regulatory milestones and $250.0 million in sales-based milestones and tiered, from mid-single to low-double digit, sales-based royalties. In 2019, Lilly invested an additional $12.0 million as part of our Series B financing.

We are also developing product candidates for the treatment of lysosomal diseases. We believe our product candidates for lysosomal diseases, including mucopolysaccharidosis type 1, or MPS-1, can leverage the well understood mechanism of enzyme replacement therapies, or ERTs, by using engineered cells to express functional human enzyme or other protein that more closely resemble normal physiology in a continuous manner. For example, our program for MPS-1 consists of product candidates that contain a cell line that is genetically modified with a nonviral vector to express human α-L-iduronidase, or IDUA, encapsulated within our spheres. In addition, we are designing our product candidates to address the neurological manifestations of certain lysosomal diseases, using molecules designed to penetrate the blood brain barrier and molecules designed to extend plasma half-life. In the first quarter of 2023, we decreased our external spend relating to our MPS-1 program to preserve capital. We expect to expand our pipeline of product candidates to include expansion areas of development, including liver disease and other validated targets, in the future.

In addition, we continue to focus on optimizing our SLTx platform technologies. In November 2021, we reported that spheres covered with pericapsular fibrotic overgrowth, or PFO, were observed during a retrieval procedure in our Phase 1/2 study of SIG-001 in severe or moderately severe hemophilia A. We have made subsequent changes to our SLTx platform, which are designed to minimize or otherwise avoid the potential for a patient's immune response to our product candidates. Our current programs, including SIG-002, have incorporated a number of these platform optimizations, including changes to our cross-linking chemistry designed to strengthen the integrity and stability of our spheres. We also developed innovative predictive preclinical models of PFO, including in vitro macrophage attachment assays and in vivo humanized mouse models to support the continued development of our product candidates, including SIG-002.



Discovery Pipeline

Following our program for diabetes, we intend to apply the SLTx platform to develop more product candidates, including product candidates for patients with liver and immune mediated diseases, and explore delivery of different molecules and alternative routes of administration. Given the modular nature of our platform, we have developed a framework for progressing to the IND-enabling phase for internal programs, which we expect to take approximately 15 to 18 months, on average, after a development candidate has been nominated. Preclinical activities include cell banking, cell culture process development, sphere optimization, and technology transfers to our contract manufacturing organizations, or CMOs. In parallel with these preclinical activities, we may request pre-IND and pre-Clinical Trial Application, or pre-CTA, meetings with the applicable regulatory authorities to incorporate their feedback in our preclinical process, for many of our products. Once preclinical materials are available, we initiate toxicology studies, pharmacokinetic studies and pharmacodynamics studies for our product candidates, *in vitro* and, later, *in vivo*. Based on the results of these studies, we may then develop a proposed clinical trial design. Prior to the completion of IND-enabling preclinical studies, we work with our CMOs to create a current good manufacturing practice, or cGMP, working cell bank, which would be expanded, differentiated to the appropriate cell type, if applicable, and encapsulated to provide the cGMP grade cell components of the clinical supply of our product candidate. This integrated process is intended to provide each program with necessary data to complete our IND and CTA applications for such program.

Strategy

Our goal is to provide functional cures to patients with chronic and acute diseases by applying our SLTx platform to discover, develop, manufacture, and commercialize a new class of medicines. To achieve this vision and maximize value to stakeholders, we are executing a strategy with the following key elements:

- **Leverage our Modular Platform.** We have focused our efforts on three core pillars of our modular platform: (i) optimization of our cell lines; (ii) optimization of our spheres; and (iii) development of scalable and cost-effective manufacturing processes. The optimization of our cell lines and spheres includes strategies to develop hypoimmune cell-based products that are designed to minimize or otherwise avoid a patient's immune response to our product candidates. In addition, we are developing innovative predictive preclinical models of PFO, including in vitro assays to further validate the hypoimmunity of our cell lines. By leveraging these components, we believe that this strategy will enable us to pursue numerous product candidates in a capital efficient manner.

- **Focused Indication Prioritization.** Following our program for diabetes, we expect to prioritize new product candidates based on the potential to provide meaningful clinical benefit to patients, rapid time to proof-of-concept, a clear regulatory path, and validated biological and clinical endpoints. In the future, we expect to target therapeutic areas in acute or chronic diseases outside of diabetes.

- **Further Strengthen our Differentiated, Proprietary and Cost-Effective Manufacturing Capability**. We have designed our manufacturing processes for reproducibility, flexibility, speed and low cost of goods. In addition, we have demonstrated our ability to scale up our manufacturing processes for our Phase 1/2 studies. We expect to continue to invest in our manufacturing platform and leverage our modularity as we further scale up our proprietary processes. We believe that, at commercial scale, the cost of goods for some of our programs will be significantly lower than existing cell or gene therapies.

- **Driving Innovation with our Strong Patient First Culture.** Since our formation, we have established a highly collaborative, patient first culture that drives our passion for innovation. Our patient first culture has allowed us to understand the needs of patients and their caregivers, including the need for innovative medicines. We have leveraged our pioneering science and our location to attract scientific talent and experienced leaders, which underscores our commitment to the patient communities we serve. In addition, we have assembled a board of directors and scientific advisors with deep expertise in research, development, regulatory affairs and manufacturing across the therapeutic areas that we are initially targeting, and that are guided by the needs of the patient community.

- **Maximizing Value Creation.** We have assembled a management team with experience in the development and commercialization of therapeutics globally, particularly in rare diseases. In other more prevalent acute or chronic diseases, we believe that executing targeted strategic partnerships for select indications or regions of the world would be beneficial to expand and accelerate access of our technology to broader patient populations worldwide, as demonstrated by our partnership with Lilly.

Limitations of Gene and Cellular Therapies

Many diseases are a result of loss or dysfunction of cells or a component produced by these cells. The loss or dysfunction can occur as a result of an inherited genetic defect or occur later in life due to several factors such as autoimmunity. There is a long history in the medical community of replacing missing or defective cells, from blood transfusions to bone marrow transplants, activated immune cells in oncology and cadaveric islet cells for T1D. There are two broad classes of cell therapy: autologous, whereby cells are obtained from the patient, and allogeneic, whereby cells are obtained from a third-party human donor. Despite the major developments and improvements in the industry, both types of therapies are associated with challenges related to acquisition of cells, manufacturing, clinical utility and safety.

Immune rejection is primarily a contact-dependent cell mediated process. A challenge to the therapeutic use of allogeneic cells has been the targeted destruction of the cells by the host immune system unless patients are treated with an immunosuppressive regimen. One strategy employed to prevent immune rejection, outside of immune suppression, is the encapsulation of cells to prevent immune cell contact. Encapsulation using biopolymers such as alginate have been extensively studied, including in human clinical trials. While these systems proved safe, the functionality was lost due to an immune response to the foreign biomaterial.

More recently, advances in genetics have enabled the engineering of cells to increase function or produce therapeutic molecules. These techniques can be applied to either autologous or allogeneic cell products. A recent example of autologous cell therapy is chimeric antigen receptor T cells, or CAR-Ts, used for the treatment of particular cancers. This has spurned much activity in the expanded utility for cell therapy. However, the use of these types of therapies is limited by a range of issues, including:

- **Limited Therapeutic Application.** Given the specialized nature of cell therapies, they have been designed for specific indications and lack the inherent platform flexibility to be rapidly applied to therapeutics across chronic diseases.

- **Limited Durability.** Allogeneic cell therapies have had limited durability due to the fast immune rejection by the host immune system. This limitation makes these therapies less efficacious in the treatment of chronic disease.

- **Safety Concerns.** Many allogeneic cell or tissue therapies such as islet cell transplantation require lifelong immunosuppression to prevent immune rejection, which is associated with significant morbidity. The use of immunosuppression restricts their use to the most severe patients.

- **Inability to Scale in a Cost-Effective Manner.** Autologous cell therapies are derived from a patient's own cells to avoid rejection by the immune system. This results in a one-to-one manufacturing process for each individual patient, which is costly and difficult to scale, and requires a complex supply chain that can delay treatment for critically ill patients.

Gene therapy is used to repair a deficiency by replacing a gene of interest with heterologous expression in the body, usually with the help of a packaging virus. This therapeutic modality has had some success with delivery of systemic protein deficiencies when the transgene is packaged and delivered via a viral vector or messenger RNA. Local gene delivery in the eye has proven effective in rare genetic disorders. However, a range of issues similar to those faced with cell therapies has also limited the use of viral and non-viral integrating medicines such as gene therapies and gene editing, including:

- **Pre-Existing Immunity.** Adeno-associated viruses, or AAVs, occur naturally in the environment and infect an estimated 70% of adults, which can lead to development of pre-existing immunity in many patients. This pre-existing immunity precludes patients from being eligible to enroll in clinical trials and to receive approved therapies. From a study of Hemophilia A patients, it was estimated that at least 25-40% of study subjects were excluded from treatment because of immunity to the AAV vectors used to deliver the gene therapy.

- **Durability and Variability Challenges.** The data that are available for gene therapy-based factor VIII programs have demonstrated that hFVIII levels in patients treated with gene therapy have initially risen in the first year, then expression waned over time. We believe these results suggest that the durability of gene therapy for Hemophilia A is likely limited for the average patient. Additionally, there is significant variability of expression levels between patients in the same dose cohort in these clinical studies for hemophilia patients. This makes predictability of patient response to a given dose very challenging.

- **Safety Concerns.** Potential for integration with the host genome may present unknown safety risks. In addition, off-target or unintended genetic modifications can arise from the use of gene therapies or genome editing tools. Because viral gene therapies can affect more than one type of cell, viruses may transduce cells other than the targeted cells and cause potential for other safety concerns. If this happens, healthy cells may be damaged, causing other illnesses or diseases.

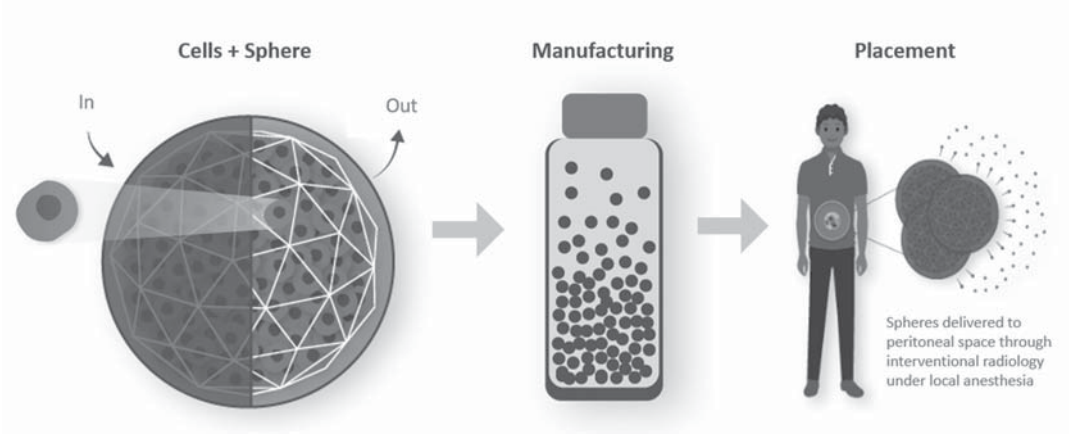
- **Inability to Redose or Remove.** Currently, certain viral gene therapies can only be delivered once due to the strong immune response to the virus, precluding repeat dosing. Once a patient receives one of these viral gene therapies, that therapy cannot be stopped, reversed or removed.

- **Limited Access Due to High Cost.** Currently, high cost of goods and high average wholesale prices are associated with gene therapies, making access to such therapies on a global basis challenging.

Our Platform - Shielded Living Therapeutics

Using our SLTx platform, our goal is to provide functional cures to patients with chronic or acute diseases. In order to overcome the limitation of existing therapies, we have developed our SLTx platform, which combines advanced cell engineering and differentiation with cutting-edge innovations in biocompatible materials to pioneer a new class of therapeutics. We are designing our product candidates to be off-the-shelf, durable, controllable and redosable, without requiring modification of the patient's genes or chronic suppression of the patient’s immune system. We engineer and/or differentiate cells, which are subsequently encapsulated in our proprietary hydrogel spheres. The spheres are composed of an outer layer comprising our Afibromer alginate, an alginate conjugated with a novel, proprietary small molecule, and an inner compartment designed to enhance cell survival and productivity. We have observed robust *in vivo* preclinical results demonstrating that the Afibromer alginate prevented the generation of an immune response against the biocompatible

spheres while enabling nutrient influx and therapeutic protein efflux. As the cells remain encapsulated in the spheres, they are designed to not interact with the host genome. We are also developing hypoimmune cell-based strategies in some programs designed to minimize or otherwise avoid a patient's immune response to our product candidates.



Our SLTx platform is comprised of two primary elements:

- **The Cells.** The allogeneic human cell lines used in our programs are selected for each indication based on their safety, durability, scalability, functionality and engineerability. We believe this approach allows us to differentiate stem cells into the appropriate cell types or, if desired, stably integrate a high-expressing transgene into an engineered cell line, with the potential, in the case of our engineered cell lines, to create a self-renewing cell population to enhance durability and manufacturing scalability. We are also generating and testing hypoimmune cells for use in some of our discovery programs.

- **The Sphere.** We encapsulate the cells in our proprietary biocompatible matrix, formatted as approximately 1.5 mm spheres, consisting of (i) an inner compartment of alginate which may be conjugated with peptide molecules to enhance cell survival and productivity and (ii) an outer hydrogel layer containing our Afibromer alginate.

In order to bring our SLTx product candidates to patients, we have designed our manufacturing process for reproducibility, flexibility, speed and low cost of goods. We use an allogeneic cell-based manufacturing process for our internal pipeline programs and follow the typical cadence of creation of a clonal master cell bank, followed by a working cell bank, and, finally, expansion of a working cell bank vial for each manufacturing run. The Afibromer alginate is created by conjugating the small molecule to the requisite alginate. Using a proprietary manufacturing process, the biomaterials are then used to encapsulate the cells, forming a sphere with the Afibromer alginate on the outside and the cells inside the sphere with the alginate biomaterial. This encapsulation process is reproducible and has been scaled for clinical development of our initial clinical product candidates. In addition, in line with other cell-based therapies, our manufacturing process provides the ability to optimize our candidate products by increasing or decreasing the volume of spheres manufactured and placed into the patient as well as the number of cells placed into each sphere. All components are manufactured under cGMP conditions by our CMOs.

Advantages of Our SLTx Platform

Our SLTx platform is designed to significantly improve the management of chronic and acute diseases by overcoming the drawbacks of current biologics-based standard of care therapies and the significant limitations of cell and gene therapies. We believe our SLTx product candidates, if successfully developed and approved, can be placed in the body and remain functional for years and potentially serve as "therapeutic factories" for diseases or conditions where a particular protein or cell is deficient. We believe our SLTx platform may provide the following potential advantages:

- **Functional Cure.** We believe that a single dose of our SLTx product candidates could provide a meaningful long-term clinical benefit to patients as well as significant health economic advantages. Our SLTx platform is designed to harness the power of cell therapies to do what these genetically modified cells are designed to do by mimicking the function of endogenous cells.

- **Controllable Dosing.** We have observed in preclinical studies that various doses of SLTx product candidates delivered consistent, dose dependent expression of the therapeutic molecules, which we believe supports predictable dosing in humans. We believe that controllable dosing has the potential to improve the safety profile of our product candidates and to better predict clinical outcomes for patients. This approach also offers the potential to tailor dosing to fit a patient's needs.

- **Redosable.** In preclinical studies, we have observed that doses of our investigational products can be administered repeatedly, if applicable, which we believe further differentiates our cell-based approach from other modalities such as gene therapy.

- **Retrievable.** While we do not anticipate a need for retrieval of our product candidates from patients, we have demonstrated in non-human primates that we can retrieve the vast majority of spheres, if necessary. In addition, in November 2021, spheres were removed or otherwise ablated in one of three patients enrolled in our Phase 1/2 clinical trial of SIG-001 in severe or moderately severe hemophilia A.

- **Off-the-Shelf.** Our SLTx product candidates are designed to be off-the-shelf, allogeneic, encapsulated cell therapies. We also believe our plans to manufacture large cryopreserved drug product lots in a fully automated encapsulation system for certain of our products will result in cost of goods significantly lower than existing cell or gene therapies with potential ability for global distribution.

- **No Integration with the Host Genome.** Our allogeneic cells are differentiated or engineered outside the body and encapsulated in spheres. Upon placement of these spheres into the body, our cells remain inside of the spheres and do not interact with the host genome or circulate in the body. This feature is designed to avoid safety issues potentially caused by insertions into the host genome. In addition, our clonal cells have known integration sites for the transgene, a gene that is introduced into the platform cell line using genetic engineering techniques.

- **Avoidance of Pre-existing Immunity.** Our platform is a non-viral engineered cell-based gene therapy. Therefore, our product candidates are not affected by pre-existing antibodies to the viral based vectors used in gene therapy approaches.

Modularity of Our SLTx Platform

Modularity is a key pillar of our strategy as the SLTx platform can be rapidly adapted to new therapeutic programs using the same biomaterial components and encapsulation technology yielding an efficient engine which is being applied to multiple product candidates. We also expect to use the same parental cell line for multiple product candidates. This platform approach to development has the potential to significantly shorten the timeline and reduce the cost from product concept to IND submission. In addition, we have developed proprietary processes for producing consistent and large scale batches that are suitable for clinical development; which includes a novel process for automated continuous cell encapsulation and the potential to cryopreserve the product.

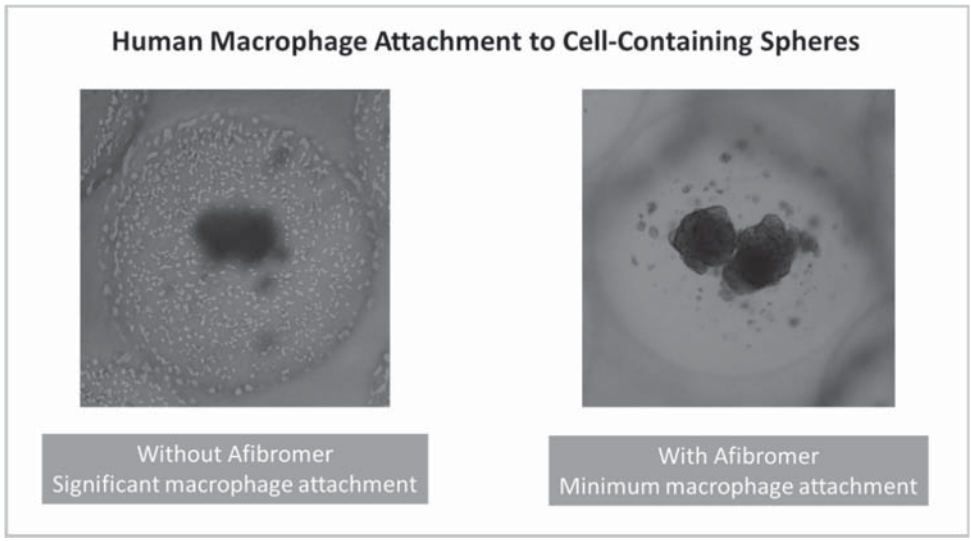
The Cells

For our current programs, we differentiate stem cells into the appropriate cell types or, if desired, stably integrate a high-expressing transgene into an engineered cell line, with the potential, in the case of our engineered products to create a self-renewing cell population to enhance durability and manufacturing scalability. For example, in our diabetes program, we are differentiating induced pluripotent stem cells, or iPSCs, into mixed populations of cell types approximating human islet cells. In the case of lysosomal disease and other programs, we engineer the appropriate cell line in a manner that does not employ viral vectors and is designed to produce an engineered cell line that expresses high levels of the desired

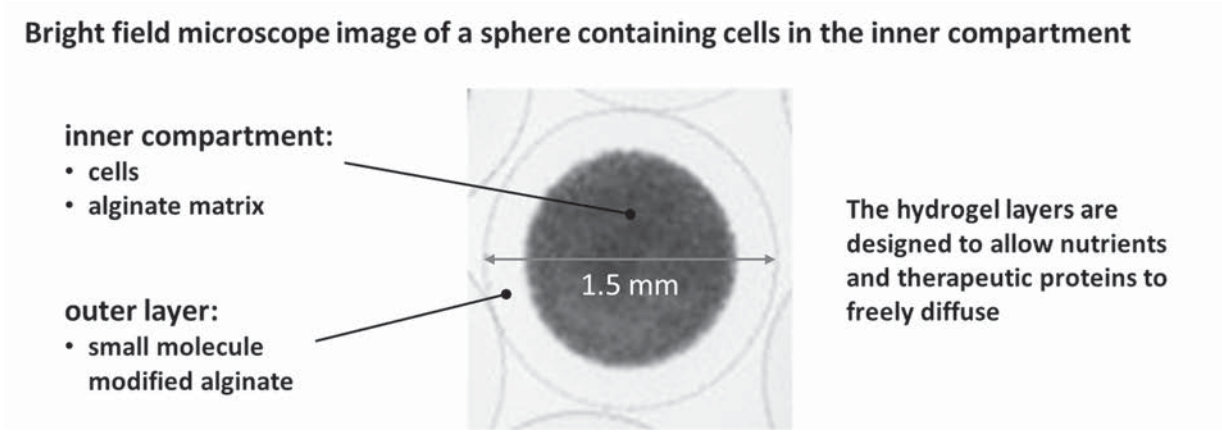
therapeutic molecule using a customized expression cassette with a heterologous transgene. Each transgene and expression cassette for these product candidates is tailored for maximal expression of the therapeutic product candidate in a continuous manner. We also optimize the promoters, insulators, polyA and signal sequences for the parental cell line, enabling us to use different transgenes. The engineered cell line is cloned, master and working cell banks are created and tested under cGMP conditions. The cells produced by our engineered cell lines have proven particularly amenable to encapsulation because they allow us to have self-renewing, long-lived population of cells. As with normal tissues, cells in the sphere have a slow turnover rate. We are also selecting for hypoimmune cells or otherwise using engineering techniques designed to minimize or otherwise avoid a patient's immune response to our product candidates.

The Sphere

Our name is derived from sigilo—a Spanish word meaning stealth. Stealth is a key attribute of our SLTx platform, which we are developing to harness the power of therapeutic cells without inducing an immune response. Our underlying technology was derived from 10 years of work in the MIT labs of Professors Robert Langer and Daniel Anderson to identify ways to prevent the foreign body response to implanted biomaterials. This work culminated in the discovery of (i) a family of novel small molecules that, when present on the surface of the alginate spheres, has been shown to prevent an immune response in preclinical studies and (ii) optimal sphere sizes. This technology is protected by a series of patents and patent applications, which we have exclusively licensed from MIT. This work, which included observations of preclinical durability in rodents and non-human primates, was described in a series of publications in Nature Journals from 2016 to 2020.



We have built upon the MIT technology to further refine the sphere configuration, composition and related manufacturing processes. We have developed a dual-layer sphere which enables us to create improved configurations for the outer layer and inner compartment. In designing the outer layer, we selected a small molecule from the MIT library, which when conjugated with the alginate, creates our Afibromer alginate that we use as an outer hydrogel coating for our spheres. We have incorporated changes to the cross-linking chemistry for Afibromer to strengthen the integrity and stability of our spheres. The inner compartment is designed to enable optimization for different cell types and to promote the viability and productivity of the encapsulated cells. The alginate, small molecule and the Afibromer alginate are all sourced and manufactured under cGMP conditions.



The Manufacturing Process

We have spent significant time and resources since we began substantial operations in 2017 to create a state-of-the-art manufacturing platform that is modular for all product candidates developed using our cell and sphere components. Each of the major components of the SLTx products, including the small molecule, the cell banks, outer layer matrix, inner layer matrix, the cellular drug substance and the encapsulated drug product, is manufactured under cGMP conditions. We have performed significant process development work in house with a longer-term vision to provide scalable and cost-effective approaches for each of these components at commercial stage. The process for manufacturing each component is independent from other components and does not differ significantly by program except for the cellular drug substance. We believe this initial groundwork will substantially enable acceleration to the clinic for future programs.

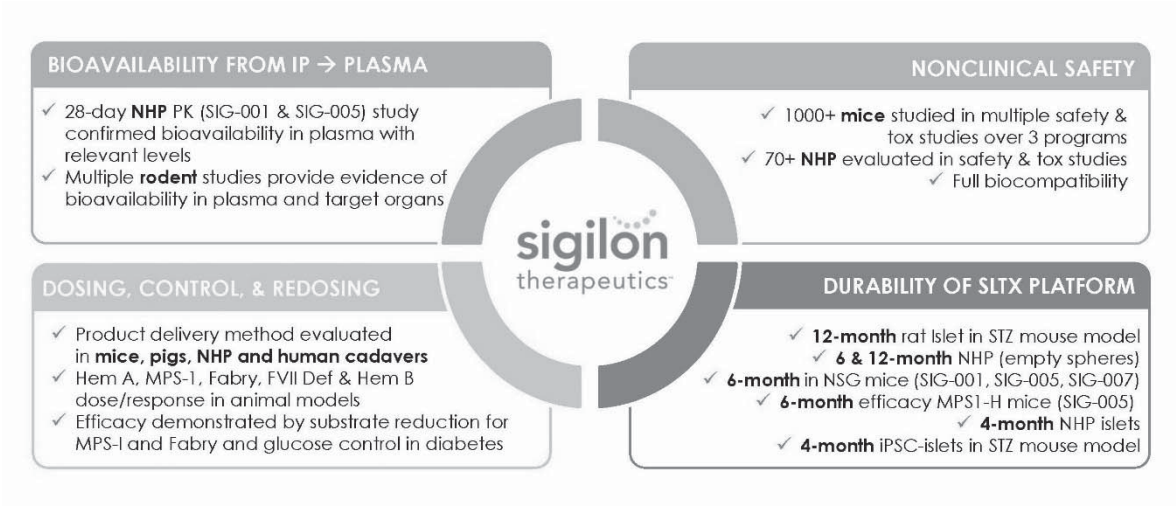
For sphere manufacturing for all programs, we use a dual lumen needle to generate the sphere. The cells with their matrix are in the inner lumen, while the Afibromer is in the outer lumen. As the droplet is pulled from the needle it hits a bath where crosslinking occurs forming a dual layer sphere. We have designed this encapsulation process for reproducibility, flexibility, speed and uniformity across all programs. We have further developed a cryopreservation process for the cellular drug substance of certain of our products. This allows us to decouple the drug substance and drug product manufacturing for such products, which we believe can reduce the lead time for drug product manufacturing by approximately 80%.

As we advance our programs, we are focusing on three key manufacturing areas: scaling up cellular drug substance manufacturing, automating and scaling up encapsulation processes, and cryopreservation of drug product. These strategic initiatives will enable a true off-the-shelf product. In addition, these investments in our manufacturing platform should enable us, at scale, to achieve commercial cost of goods significantly lower than current approved cell therapies on the market. We believe the cost of our treatment for certain programs can be significantly lower than existing cell or gene therapies, if our product candidates are approved.

Foundational data on our SLTx platform

We have performed several safety and durability studies using sphere components for our internal programs. Third-party *in vivo* studies have shown that alginate spheres of similar composition can remain intact in the body for over nine years with no reported adverse effects. In extensive preclinical testing for our initial programs, conducted with our first generation sphere composition to support our regulatory filings, we observed no toxicity. Chronic toxicity and local tolerance testing showed that the sphere components were well tolerated in Non-Human Primates, or NHPs, up to 12 months. In addition, empty spheres using this composition were not found to be sensitizing, cytotoxic, mutagenic, an irritant, or pyrogenic. The intraperitoneal administration of empty or high and low dose spheres containing cells was well tolerated, with no adverse control or test article-related effects observed in long-term safety studies. The spheres used in our initial preclinical programs were also observed to be biocompatible and our product candidates were shown to be non-cytotoxic and non-mutagenic in preclinical studies. We also observed no acute systemic toxicity following injection of empty sphere extracts in mice. These preclinical safety studies were completed for our programs in Hemophilia A and

MPS-1 and regulatory agencies have acknowledged the potential to leverage these data in subsequent filings for other product candidates. Below is a summary of the relevant preclinical studies.



Six-month and twelve-month NHP Study. We examined chronic toxicity and local tolerance of a single dose of empty spheres at doses at least 5x higher than the expected maximum human dose in Cynomolgus monkeys by administration into the bursa omentalis or into the general peritoneal space via implantation through an endoscopic trocar. There were no empty sphere-related toxicities observed on clinical pathology endpoints in Cynomolgus monkeys at either six months or 12 months after administration. The empty spheres implanted into the intraperitoneal cavity were well tolerated with no notable adverse effects.

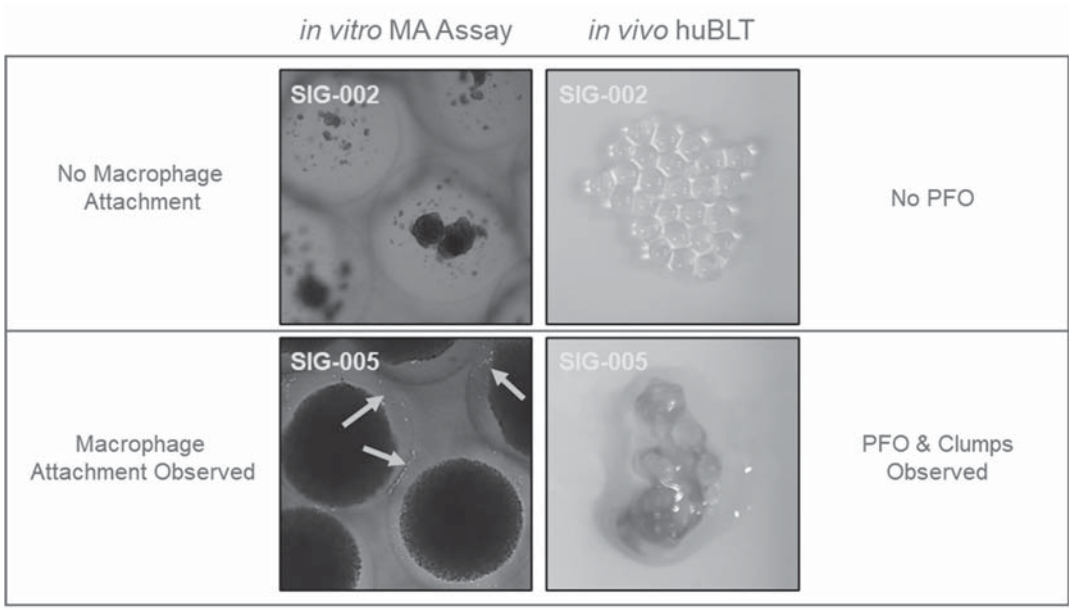
Broken Sphere Study. An additional sphere tolerability study was conducted upon regulatory agency request in which we broke 50% of the spheres including cells prior to implantation to mimic a worst-case scenario for sphere integrity. An independent toxicology report found no adverse findings of note including any issues with the cells which were artificially enabled to escape the sphere *in vivo*.

Mode of Delivery

We have explored a variety of anatomical locations for systemic or local delivery of our product candidates. For our first programs in rare blood disorders, where large levels of systemic protein are required, we selected the general peritoneal space delivery through a laparoscopic trocar/catheter. This minimally invasive surgical procedure can be performed under general anesthesia in most patients in less than 30 minutes. Nevertheless, in addition to laparoscopy procedure, we developed a simplified procedure for sphere administration into the peritoneal cavity using minimally invasive techniques, such as interventional radiology guided placement. We believe this delivery method has several advantages over other forms of minimally invasive surgery, including local anesthesia and a single incision point. For indications in which smaller amounts of therapeutics will be required, such as immune-mediated conditions, we are developing alternative routes of administration.

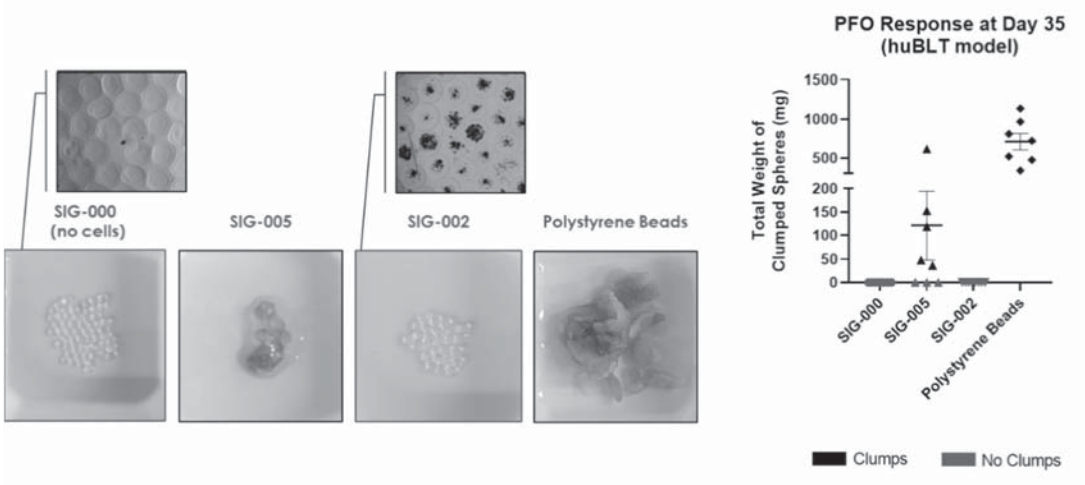
Pericapsular Fibrotic Overgrowth, or PFO, Prediction Methods

We have developed proprietary methods to evaluate the potential for PFO of our product candidates in preclinical models. These methods include initial testing using a novel assay designed to measure macrophage attachment to our product candidates (as shown by red dots below). If this screen results in little to no macrophage attachment, product candidates are then tested in a humanized mouse model using positive controls for PFO (as measured by the amount of clumping below), such as polystyrene beads or encapsulated cells known to generate PFO. If no PFO is observed in these comparative studies, then product candidates may be evaluated for pharmacokinetics and toxicology in non-human primates.



We have used these preclinical models to evaluate our product candidates including SIG-002, our product candidate for diabetes, with our improved cross-linking chemistry. The humanized BLT, or hu-BLT, mouse model recapitulates important aspects of a human immune system, including the myeloid lineage, to assess both adaptive and the innate immunity. PFO presents as "clumping," or the adherence of cellular material to the spheres, in the hu-BLT model and, therefore, we believe models our clinic observations of PFO. Specifically, in hu-BLT studies, significant clumping was evident in hu-BLT mice containing polystyrene beads, as shown in the figure below, which serves as a positive control for these studies. In contrast, no clumping or evidence of PFO was observed in hu-BLT mice containing empty spheres, also referred to as SIG-000. We have also evaluated spheres in hu-BLT mice containing two different types of cellular product: (i) SIG-002, which contains differentiated iPSCs, and (ii) SIG-005, which contains epithelial cells engineered to produce therapeutic protein, but not otherwise engineered to be hypoimmune. Importantly, we observed no clumping or evidence of PFO in hu-BLT mice containing SIG-002. We observed mild clumping, or a mild PFO response, in hu-BLT

mice containing SIG-005. Using this data, we are moving forward with non-human primate and IND-enabling activities for SIG-002 in the second half of 2023. We are also evaluating the use of other cells derived from iPSC, such as hepatocytes.



Type 1 Diabetes

SIG-002 is an islet cell replacement therapy product candidate for the treatment of T1D. In T1D, the immune system attacks and destroys the insulin-producing beta cells within the endocrine islets of the pancreas. Insulin deficiency results in dysregulation of glucose metabolism. In April 2018, we partnered with Lilly to develop cell therapies for the treatment of T1D, including SIG-002.

Indication / opportunity

T1D is an autoimmune and chronic disease that results from the destruction of pancreatic beta cells. T1D patients are unable to produce sufficient levels of insulin to effectively modulate glucose levels and require subcutaneous insulin injections and regular blood glucose monitoring to maintain blood glucose levels within an appropriate range. There have been advances with different insulins, insulin pumps and continuous glucose monitoring that have improved management. Nonetheless, less than one-third of people with T1D in the United States are consistently achieving target blood glucose control levels. Vascular damage from chronic elevated blood glucose levels can result in various complications including neuropathy, retinopathy, nephropathy, and cardiovascular disease. Some T1D patients, usually described as having brittle diabetes have chronic severe metabolic instability despite intensive insulin therapy; this includes patients with a history of multiple episodes of severe hypoglycemic events, or SHEs, often with impaired awareness of hypoglycemia, or IAH.

Recent estimates indicate that in the United States approximately 1.45 million people have T1D and that number is projected increase to 2.1 million by 2040. Despite advances in blood glucose monitoring and insulin delivery technologies, there is a need for improved treatments for T1D. Specifically, we believe there is a need for a functional cure, something to replace the pancreas. While fluctuations in blood glucose levels have been reduced with pancreas or islets transplantation and some patients became independent of exogenous insulin administration, immunosuppression is needed to preserve effectiveness of these treatments. There are approximately 1,000 pancreatic transplants performed annually in the United States.

Limitations of Current Therapies

T1D patients require subcutaneous insulin injections to maintain blood glucose levels within appropriate range. Despite recent advances in a range of therapeutic options with exogenous insulin and glucose monitoring, a significant unmet clinical need remains for people with T1D. A large majority of adults and adolescents with T1D do not meet HbA1c management goals, and substantial rates of life-threatening severe hypoglycemia and diabetic ketoacidosis persist, as

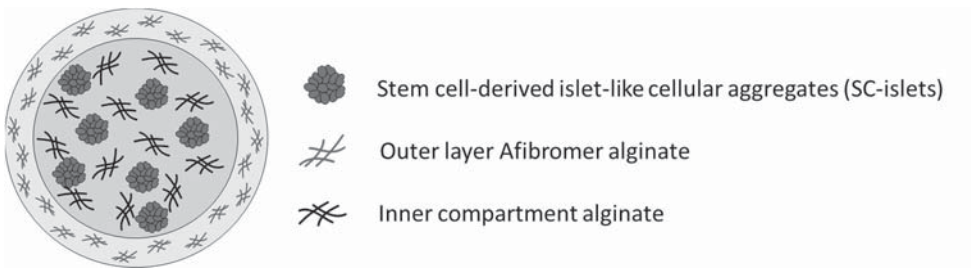
recently reported by the T1D Exchange Registry. High risk T1D patients have chronic severe metabolic instability despite intensive insulin therapy; this includes patients with a history of multiple episodes of SHEs, often with IAH.

High risk T1D patients are candidates to receive cadaveric allogeneic pancreatic islet cell products or pancreatic transplants. Allogeneic islets are typically transplanted into the portal vein along with an immunosuppression regimen to prevent allograft rejection. A Phase 3 clinical trial in subjects with intractable IAH and SHEs demonstrated that allogeneic islet transplantation provided glycemic control, restoration of hypoglycemia awareness, and protection from SHEs. Forty-two percent of subjects achieved insulin independence for at least two years. Adverse safety events reported were related to the infusion procedure and immunosuppression, including bleeding and decreased renal function. A shortage of donor cadaveric islets and the need for chronic immunosuppression preclude wider use of cadaveric islet transplantation therapy for T1D.

Our Solution—SIG-002

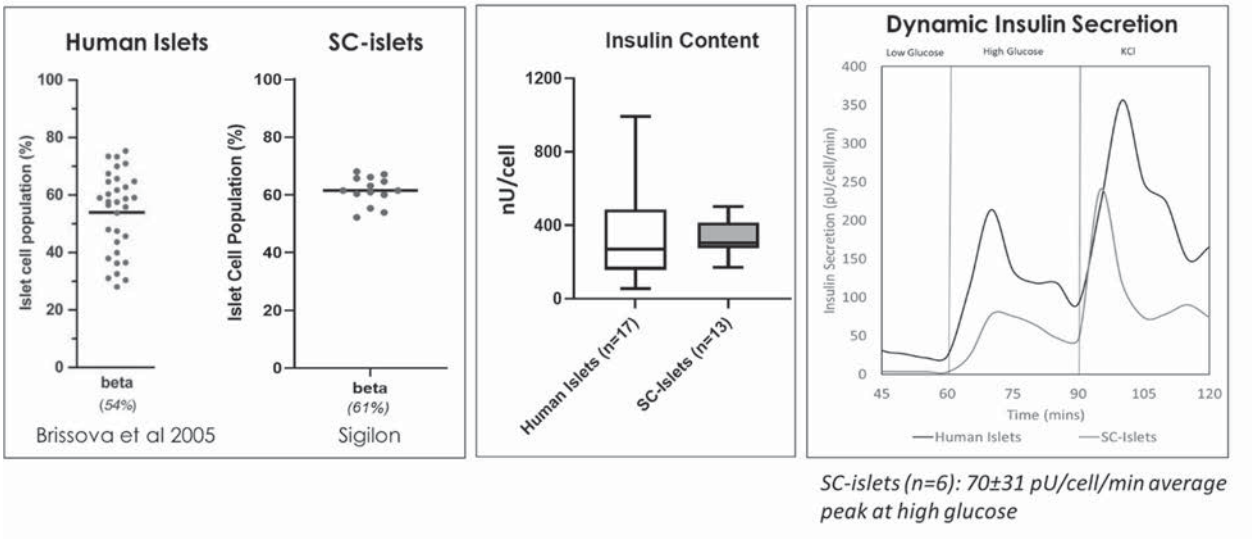
SIG-002 is in development for individuals with T1D who have difficulty regulating their blood glucose levels using available insulin therapies. SIG-002 is designed to improve glycemic control, thereby reducing complications of T1D and improving quality of life outcomes for patients. SIG-002 comprises an allogeneic endocrine cell population, which we prepare by differentiating induced pluripotent stem cells, or iPSCs, using a proprietary protocol designed to produce cells that function similarly to human islets with glucose-responsive, insulin-secreting cells (SC-islets). The differentiated cells are encapsulated within our spheres to prevent immune rejection of the cells, as illustrated in the figure below. We are developing SIG-002 under our partnership with Lilly and, except for certain activities taken on by Lilly, we are leading the execution of research and development activities until the first IND filing.

SIG-002 Drug Product Sphere



SIG-002 has the potential to regulate blood glucose homeostasis through glucose-responsive secretion of insulin from the alginate spheres, or sense and respond. SIG-002 is designed to provide durable insulin secretion.

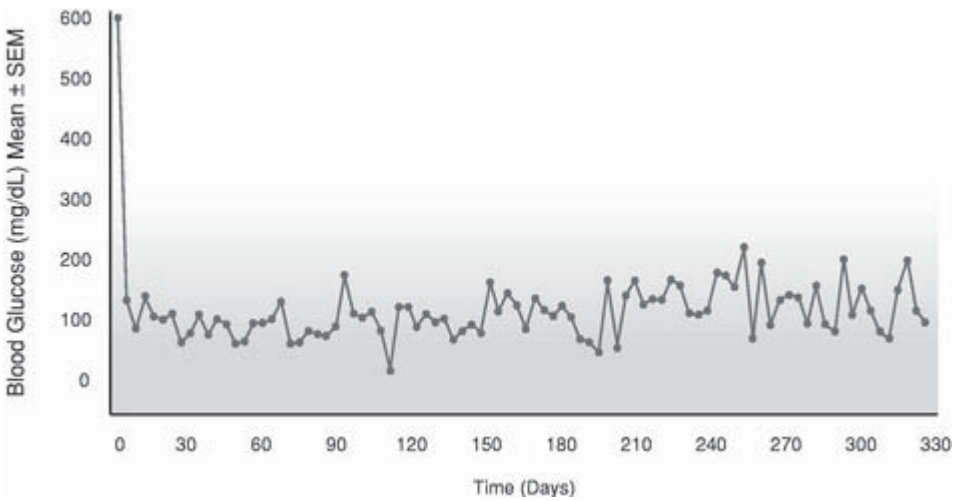
In collaboration with Lilly, we have acquired induced pluripotent stem cells, or iPSCs, that we have differentiated to pancreatic islets using a multi-step protocol. These allogeneic human SC-islets are then encapsulated in our spheres. We have developed a proprietary differentiation protocol that is reproducible, with scalable processes for cGMP manufacturing. With flow cytometry analyses we have shown that our protocol generates SC-islets with a high percentage of beta cells (c-peptide-positive/glucagon-negative), on average 61%. Further, our SC-islets have insulin content levels that are comparable to human islets and show glucose-responsive insulin secretion. In comparison to human islets, our data show we can produce SC-islets with more consistent cell populations.



Foundational Data

Early experimental data demonstrated that even with xenogeneic cells from different species, rat islets, shielded with Afibromer technology, remained functional for long periods of time, normalizing glucose control in streptozotocin-induced diabetic mice.

In this study, MIT implanted 0.5 ml of one-layered spheres containing rat islets in the peritoneal cavity of healthy mice, treated with streptozotocin, or STZ, to invoke diabetes. Mice were then tested for blood glucose levels every three days for 330 days until the mice were sacrificed. This experiment was repeated three different times with similar results each time with cohorts of five mice, consistently achieving blood glucose measures under 200mg/dL, normal blood glucose level for mice. In addition, in another MIT study, human islets differentiated from embryonic stem cells were placed into STZ mice and, in this study, normal blood glucose levels were maintained in mice for the duration of the study.



Rat donor islets in STZ mice.

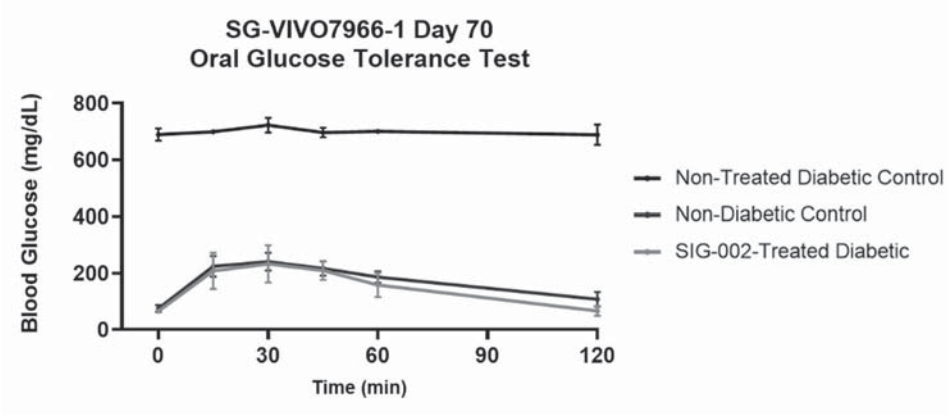
SIG-002 Preclinical data

We have developed a robust preclinical program for SIG-002, including studies designed to support the biocompatibility of the alginates, as well as to evaluate the efficacy and safety of the product candidate. These studies are designed to address the following preclinical objectives:

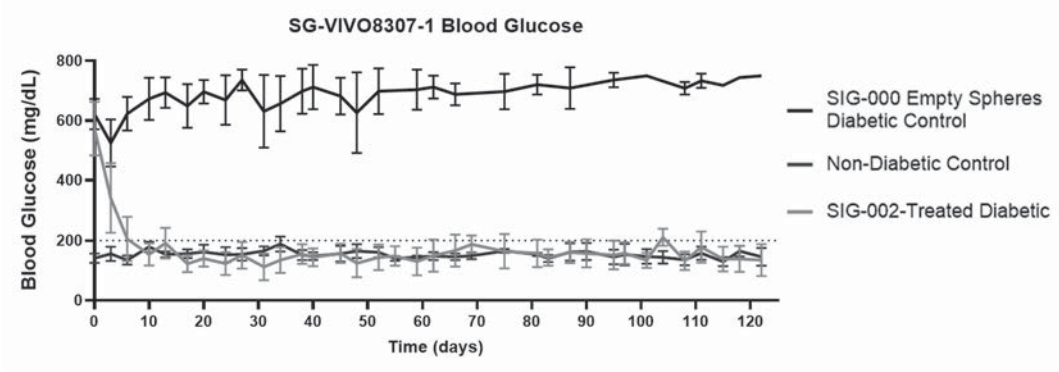
- Evaluation of long-term efficacy of the intended clinical product candidate in a murine model of diabetes with assessment of multiple doses; and

- Safety assessment of intended clinical product candidate.

In preclinical studies, we have shown that SIG-002 was efficacious in the STZ-induced diabetes mouse model. As shown in the figure below, after 10-weeks *in vivo*, SIG-002-treated immunocompromised mice effectively cleared an oral glucose challenge (1g/kg) after an overnight fast.

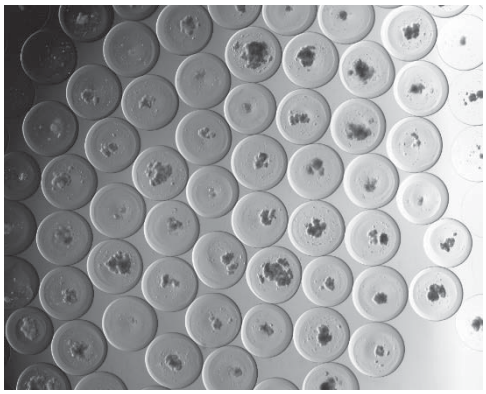


Further, we have shown that SIG-002-treated, STZ-induced diabetic, immunocompromised mice maintained normoglycemia with blood glucose levels comparable to non-diabetic control mice and with human c-peptide in the plasma for up to four months.



In addition to our preclinical studies, we are optimizing the scaled manufacturing processes for SC-islets and SIG-002 spheres. Unlike the cells in our other product candidates, SC-islets are in cellular aggregate form rather than individual cells. We believe our efforts are important to create a standard manufactured sphere with a uniform number of SC-islets per sphere.

SIG-002: Encapsulated SC-islets



Clinical Development Plan

We are currently working through the IND-enabling preclinical studies described above in collaboration with Lilly. Lilly is responsible for the clinical development of SIG-002, including establishing a clinical development plan.

Lysosomal Diseases

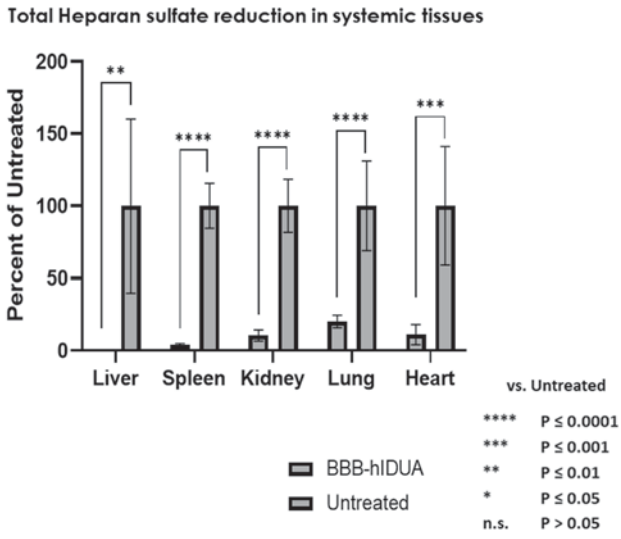
Lysosomal diseases are a large group of nearly 50 diseases affecting lysosomal enzyme function and resulting in the accumulation of substrates within cells leading to progressive impairment of their function. The age of manifestation and speed of progression varies depending on the underlying disorder and amount of residual lysosomal enzyme activity. Lysosomal diseases may affect different organ systems, including the skeleton, brain, skin and soft tissues, joints, heart, and CNS and symptoms are chronically progressive. At present, enzyme replacement therapy, or ERT, hematopoietic stem cell transplantation, or HSCT and substrate reduction therapy are available treatment options for patients with certain types of lysosomal diseases.

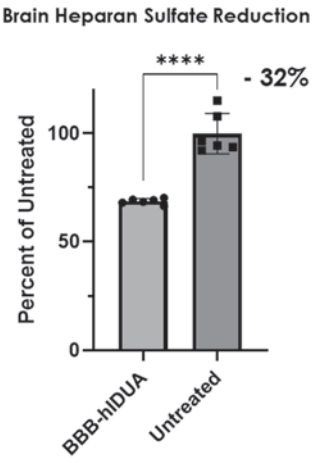
Lysosomal diseases such as Fabry disease, Gaucher disease and several mucopolysaccharidoses, or MPS, are primarily managed by frequent, multi-hour infusions with ERTs that seek to exogenously replace the dysfunctional enzyme. However, given the characteristics of most ERTs, they require frequent dosing. These existing therapies have made a positive impact on these patients, but, as the dosing and frequency have not been optimized, the dosing does not resemble physiological conditions and diseases may progress or be ineffectively managed. Further, the frequent, periodic and life-long dosing schedule required for ERTs results in significant costs for the healthcare system and is burdensome for the patient. While biopharmaceutical companies are considering gene therapies for the treatment for several diseases caused by single genetic defects, this approach has historically exhibited unpredictable dose response and potential long-term safety concerns, including genotoxicity.

We believe our SLTx therapies can leverage the well-understood mechanism of ERTs by using engineered cells to express functional enzymes or other proteins that more closely resemble normal physiology in a continuous manner. We believe that a single dose of our SLTx therapies may provide meaningful longer-term benefit to these patients and functionally cure these diseases while also providing significant health economic advantages.

In December 2021, we announced a strategic reprioritization focusing our development efforts on diabetes and MPS-1. In the first quarter of 2023, we decreased our internal and external spending relating to our MPS-1 program to preserve capital. We are also developing next generation product candidates to address the neurological manifestations of mucopolysaccharidoses, such as MPS-1, using transporter molecules designed to penetrate the blood brain barrier, or BBB, and molecules designed to extend plasma half-life. In preclinical studies, cells engineered to express human α-L-iduronidase, or IDUA, for the treatment of MPS-1 demonstrated sustained substrate reduction in peripheral organs, such as the liver, spleen, kidney lung and heart as measured by reductions in heparan sulfate. More importantly, in this 21-day study, there was also a significant level of substrate reduction in the central nervous system reflecting the transporter

molecules ability to cross the BBB. Our ability to leverage the modularity of our SLTx platform and manufacturing processes across our lysosomal disease programs is expected to result in a streamlined path for these programs to the clinic.

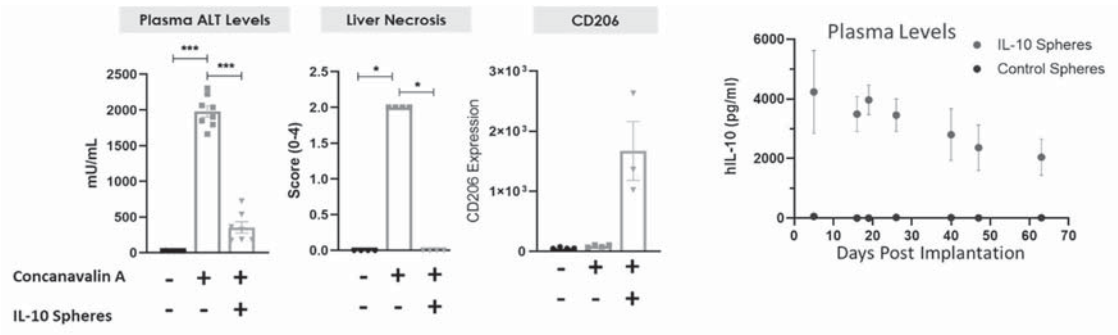


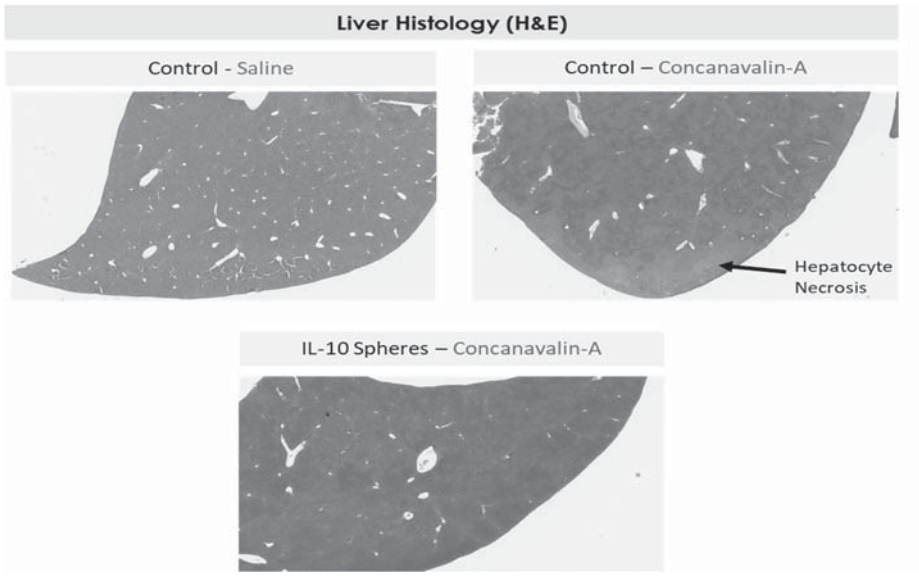


Liver diseases

We believe that our SLTx platform has the potential to provide a functional cure to patients with liver diseases by restoring function through the production of proteins (A1AT, albumin) and detoxifying disease-causing metabolites (ammonia, urea, and xenobiotics) or by reducing hepatic cell death.

We are currently exploring targets and indications most suitable to benefit from our platform technology. Preclinical data has shown our product candidates can overcome pharmacokinetic barriers hampering the therapeutic use of certain treatments, potentially providing treatments for a number of diseases with high unmet need. As proof of concept, we have shown that we can produce a wide variety of these important modulators. For example, in a murine model of autoimmune hepatitis, we have demonstrated that cells engineered to produce a sustained level of IL-10 in the plasma, are able to modulate the immune system towards a more immunosuppresive phenotype as measured by CD206 expression on peripheral blood monocytes. The induction of this phenotype through delivery of IL-10 was also associated with the reduction of hepatic cell death as determined by histology and plasma alanine transaminase, or ALT, levels, a marker of liver damage.



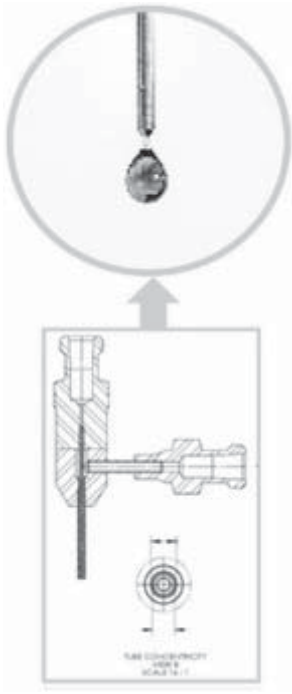


Manufacturing Process

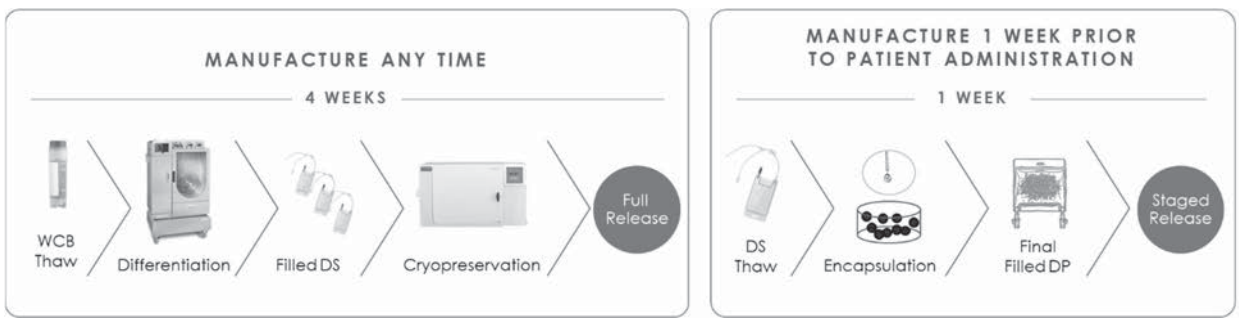
We have spent significant effort and resources to create a standardized, efficient, flexible, and consistent manufacturing platform. Our cellular drug substance manufacturing process follows the typical biologics manufacturing cadence of creation of a clonal master cell bank, followed by a working cell bank, and, finally, expansion and differentiation of a single working cell bank vial for each manufacturing run. The hydrogel and Afibromer alginate are sourced and manufactured in compliance with cGMPs by our CMOs and are used for all of our programs. We believe the modularity of our platform approach allows us to reduce the time from product concept to IND since the manufacturing know-how and preclinical testing can be leveraged from therapy to therapy. The cost of goods for certain product candidates, if approved, is expected to be significantly lower than the cost of existing cell or gene therapies, and given the durability of treatment, the cost of goods has the potential to be significantly lower than existing cell or gene therapies.

Consistent with other cell therapies, we have designed our manufacturing process to provide the flexibility to refine our product candidates to optimize the therapeutic dose for patients. We believe these refinements could include increasing or decreasing the number of spheres manufactured and placed into the patient as well as the number of cells placed into each sphere. In addition, we continue to explore opportunities to improve cell potency through process development changes designed to enhance cell function. For example, by changing our wash and storage buffer, we have seen an increase in cell potency over the prior buffer. We will continue to explore these types of enhancements and will implement them when we believe appropriate.

The encapsulation process to generate final drug product is unique and proprietary to the SLTx platform and the critical step in creating our product candidates. We manufacture the spheres using a dual lumen needle. The cells with their matrix are in the inner lumen, while the Afibromer alginate is in the outer lumen. A droplet is then emitted from the needle, drops into a bath, where crosslinking of the polymers is induced to form spheres with long term stability and integrity. The dual layer sphere has the cells in the inner compartment while the small molecule biomaterial is in the outer layer which has contact with the body.



Currently we use a proprietary semiautomated process for encapsulation. The final product is shipped at room temperature. We plan to develop a fully automated encapsulation system, which is expected to include cryopreserved final drug product. We also believe these manufacturing innovations and know-how will enable us to have allogeneic cell therapies with a cost of goods for certain products significantly lower than existing cell or gene therapies.



Competition

The biotechnology and pharmaceutical industries, including the cell and gene therapy field, are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. Any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our technology, development experience and scientific knowledge in the field of cell and gene therapy and manufacturing provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions.

There are numerous companies that are selling or developing genetic medicines that may directly compete with our SLTx product candidates. These companies include Sanofi, Takeda, BioMarin, Novo Nordisk, Sangamo Inc., or

Sangamo, Spark, Inc., or Spark, Ultragenyx, Pfizer, Bayer, UniQure, Inc., or UniQure, CSL Behring, Freeline Therapeutics Holdings plc, or Freeline, Roche and Vertex Pharmaceuticals, Inc.

Many of our competitors, either independently or with strategic partners, have substantially greater financial, technical and human resources than we do. Accordingly, our competitors may be more successful than we are in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approval for treatments and achieving widespread market acceptance. Merger and acquisition activity in the biotechnology and biopharmaceutical industries may result in resources being concentrated among a smaller number of our competitors. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials and acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunity could be substantially limited if our competitors develop and commercialize products that are more effective, safer, less toxic, more convenient or less expensive than products we may develop. In geographies that are critical to our commercial success, competitors may also obtain regulatory approvals before us, resulting in our competitors building a strong market position in advance of the entry of our products. In addition, our ability to compete may be affected in many cases by insurers or other third-party payers seeking to encourage the use of other drugs. The key competitive factors affecting the successful of all any products we may develop are likely to be their efficacy, safety, convenience, price and availability of reimbursement.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our platform technology, programs and know-how related to our business, defend and enforce our intellectual property rights, in particular, our patent rights, preserve the confidentiality of our trade secrets and operate without infringing valid and enforceable intellectual property rights of others. We seek to protect our proprietary position by, among other things, exclusively licensing and filing United States, or the U.S., and certain foreign patent applications related to our platform technology, product candidates and improvements that are important to the development of our business, where patent protection is available. We also rely on trade secrets, know-how, continuing technological innovation and confidential information to develop and maintain our proprietary position and protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Our in-licensed patents and patent applications cover various aspects of our SLTx platform, including chemically-modified alginates, methods of encapsulation and sphere compositions. We also have filed patent applications directed to the composition, configuration and manufacturing of our spheres. In addition, we have filed, or plan to file when appropriate, patent applications directed to the specific therapeutic protein expression construct and/or cell line used in each of our product candidates. We intend to pursue, when possible, additional patent protection, including composition of matter, method of use and process claims, directed to future product candidates and improvements to our SLTx platform, including manufacturing of individual sphere components and sphere preparations.

Notwithstanding these efforts, we cannot be sure that patents will be granted with respect to any patent applications we have licensed or filed or may license or file in the future, and we cannot be sure that any patents we have licensed or patents that may be licensed or granted to us in the future will not be challenged, invalidated or circumvented or that such patents will be commercially useful in protecting our technology. Moreover, trade secrets can be difficult to protect. While we have confidence in the measures we take to protect and preserve our trade secrets, such measures can be breached, and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. For more information regarding the risks related to our intellectual property, please see Part I, Item 1A "Risk Factors" — "Risks Related to Our Intellectual Property."

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. Also, the term of a U.S. patent relating to an approved drug product may be extended pursuant to the Drug Price Competition and Patent Term Restoration Act of 1984; however, an extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug or a method for using it may be extended.

As of December 31, 2022, we owned two patents (one patent in each of Australia and Singapore) and have 145 pending applications, including six pending U.S. provisional patent applications, 11 pending PCT patent applications, 15 pending U.S. non-provisional patent applications, 14 pending European patent applications and 99 other related patent applications in jurisdictions outside the United States and Europe. These patent applications relate to the composition, configuration, manufacturing and methods of use of all elements of the SLTx platform and our product candidates. If issued as U.S. patents, and if the appropriate maintenance fees are paid, the U.S. patent applications would be expected to expire between 2037 and 2043, excluding any additional term for patent term adjustments or patent term extensions.

Aspects of our SLTx platform technology are covered by patents and patent applications licensed from MIT on an exclusive or non-exclusive basis. The exclusively licensed MIT portfolio includes several patent families that cover our Afibromer matrix and the dual-layer configuration used in our spheres. As of December 31, 2022, our exclusively licensed MIT portfolio related to our SLTx platform consisted of: 20 U.S. patents; two European patents and related validations; 25 patents in jurisdictions outside the United States and Europe and 19 pending patent applications, including three pending U.S. non-provisional patent applications; and six pending European patent applications. The patents and patent applications outside of the United States and Europe are held primarily in Australia, Canada and Japan, although some of our in-licensed patent families were filed in a larger number of countries. As of December 31, 2022, our non-exclusively licensed MIT portfolio related to our SLTx platform consisted of one U.S. patent. The claims from our in-licensed portfolio include claims to compositions of matter, methods of use and certain processes. Our current in-licensed U.S. patents, if the appropriate maintenance fees are paid, are expected to expire between 2032 and 2038, excluding any additional term for patent term adjustments or patent term extensions. If issued as U.S. patents, and if the appropriate maintenance fees are paid, the U.S. patent applications would be expected to expire between 2032 and 2036, excluding any additional term for patent term adjustments or patent term extensions.

License and Collaboration Agreements

Exclusive Patent License Agreement with the Massachusetts Institute of Technology

In February 2016, we entered into a license agreement with MIT, together with all amendments, the MIT License, pursuant to which we received an exclusive, worldwide, royalty-bearing license under certain patent rights owned or controlled by MIT to develop, make, have made, use, offer to sell, sell, lease, import and export products, and to develop, perform, practice, sell and offer to sell processes, in the field of the diagnosis, treatment and/or prevention of disease or other conditions in humans and animals.

Under the MIT License, we are obligated to use commercially reasonable efforts to develop licensed products or licensed processes and to introduce such products or processes into the commercial market, making them reasonably available to the public. There are also certain developments, spending and fundraising milestones that we are required to meet, as well as timelines for the completion thereof.

MIT and Boston Children's Hospital retain the right on behalf of themselves and other non-profit research institutions to practice under the licensed patent rights for non-profit research, teaching and educational purposes, including sponsored research and collaborations. The U.S. government also retains a non-exclusive license to practice any government funded invention claimed in any licensed patent. The Juvenile Diabetes Foundation retains the right to use

and practice certain patent rights for non-commercial research purposes related to the diagnosis, cure, treatment and/or prevention of T1D and its complications.

Although the licenses granted to us under the MIT License are exclusive, MIT may grant a license to a third party under the licensed patents to develop and commercialize a product or process in the field under limited circumstances. If a third party inquires with MIT or us for such a license, the party receiving the inquiry will obtain a proposal summary from such third party and notify the other party of such proposal. If we do not (i) reasonably demonstrate that (1) the proposed product would be directly competitive with a licensed product or process that we, our affiliates or sublicensees are diligently developing, (2) we, our affiliates or sublicensees have already begun a project for and are diligently researching, developing or commercializing the proposed product, or (3) based on competent evidence, the third party does not have adequate financial or scientific resources or a reasonable strategy to develop and commercialize such proposed product, (ii) provide MIT with a business plan with mutually acceptable, reasonable diligence milestones for the commercial development of the proposed product or (iii) negotiate in good faith with such third party and enter into a sublicense agreement on commercially reasonable terms, MIT may grant a license to the third party and our license under the patent rights for the proposed product will terminate.

We are permitted to sublicense our rights under the MIT License through multiple tiers, provided that any such sublicense is on terms that are sufficient to permit us to comply with the MIT License. However, if we become a non-exclusive licensee for any licensed patent in any country pursuant to our discontinuation of support for such licensed patent in such country or an amendment to this agreement, we will no longer have the right to grant sublicenses under such patent right in such country.

In exchange for the licenses grant to us under the MIT License, we issued MIT 333,333 shares of common stock, paid MIT a license issue fee of $50,000 and reimbursed MIT $10,000 for past patent costs. We paid MIT an additional $15,000 improvement fee and reimbursement for past patent costs in connection with each of the 2018 and 2019 amendments to the MIT License. Pursuant to the MIT License, MIT also has the right to participate in future private equity offerings by us. We are required to pay MIT annual license maintenance fees ranging from low-to-mid five figures to low-to-mid six figures, depending on the particular calendar year. MIT is entitled to receive potential clinical, regulatory and sales milestones in the low-to-mid eight figure range.

MIT is entitled to receive low single digit royalties on our net sales of licensed products until, on a product-by-product and country-by-country basis, the expiration of the last valid claim within the patent rights covering such licensed product in such country. We are entitled to certain offsets on these royalties if we or an affiliate must pay royalties to one or more third parties in order to obtain a license necessary to make, use or sell licensed products. Our royalty payments will increase if we or our affiliates bring a patent challenge and MIT does not exercise its termination right. If we sublicense our rights to develop or commercialize a licensed product or process under the MIT License to a third party and we receive non-royalty sublicense income, then MIT is entitled to a percentage of such consideration, ranging between 10% and 20% depending on the date in which such sublicense agreement is executed and the stage of development of our licensed products at such time.

Unless earlier terminated, the MIT License will remain in effect until the expiration or abandonment of all valid claims within the patent rights. We may terminate the MIT License at our convenience following written notice to MIT. MIT may terminate the MIT License if (i) we cease to carry on our business related to the MIT License or become insolvent, (ii) we fail to make payments or commit a material breach of our diligence or other obligations under the MIT License following written notice, or (iii) we bring a patent challenge or one of our sublicensees brings a patent challenge and we fail to terminate such sublicense. Upon termination by MIT in regards to certain licensed patents related to T1D for our failure to fulfill our related diligence obligations, and at MIT's request, we will grant MIT a non-exclusive, worldwide, sublicensable license under the other licensed patents solely to the extent necessary to develop, make, have made, use, sell, offer to sell, lease, import and export products covered by such terminated patents in the field of diagnosis, treatment and/or prevention of T1D in humans and animals.

Eli Lilly Strategic Research and Development Partnership

In April 2018, we entered into a research collaboration and exclusive license agreement with Lilly for the development and commercialization of SLTx product candidates for the treatment of T1D. We formed a strategic partnership with Lilly because they are a leader in the field of diabetes and because of their industry expertise and capabilities in diabetes treatment and their experience developing and commercializing pharmaceutical products. Under this agreement, we granted Lilly an exclusive, royalty-bearing license, including the right to grant sublicenses to certain know-how and patent rights related to our SLTx technology, including patent rights licensed to us pursuant to the MIT License, to research, develop, manufacture and commercialize products comprising encapsulated islet cells, which we believe have potential use for the treatment of T1D. Lilly has granted to us a non-exclusive, royalty free license, with the right to sublicense, to use and practice certain intellectual property to research, develop, manufacture or commercialize products that do not contain islet cells, and other rights.

We are responsible for preclinical development of a product candidate, and completion of the studies and other criteria required for filing the first IND with respect to such product candidate. Lilly is then responsible for filing the first IND for a product candidate developed pursuant to the partnership and all subsequent clinical development and commercialization. Lilly is also responsible for all research, development and commercialization with respect to any subsequent product candidate. As of December 31, 2022, the most advanced product candidate in this partnership is in the pre-IND stage.

We are responsible for our own costs and expenses associated with research and development ahead of the first IND filing for a product candidate developed pursuant to the partnership. Lilly is responsible for its own costs in the development, commercialization and manufacture of the product candidates, as well as research and development costs for the first developed product candidate, above $47.5 million.

We and Lilly agreed to evaluate a third-party cell line provider to provide differentiated human pancreatic islet cells, for use in the product candidates developed pursuant to the partnership. Prior to the filings of the first IND we are responsible for all preclinical supply of the product candidates. Following submission of the first IND, we will be responsible for the supply of investigational product for Phase 1 clinical trials and, following completion of such trials, we will continue to be responsible for supplying to Lilly encapsulation material used in each product candidate for clinical and commercial use.

We received a $62.5 million upfront payment from Lilly under this agreement. If our first product candidate developed pursuant to the partnership is successfully developed and commercialized, we are entitled to receive up to $165.0 million in regulatory milestones and $250.0 million in sales-based milestones and tiered (from mid-single-to-low-double digit) sales-based royalties on net sales of such product. In connection with the 2018 Lilly Agreement, we issued to Lilly 3,500,000 shares of our Series A-3 convertible preferred stock for a purchase price of approximately $13.1 million. In 2019, Lilly purchased 2,000,000 shares of our Series B convertible preferred stock for a purchase price of approximately $12.0 million. The Series A-3 and Series B convertible preferred stock converted into common stock in connection with our initial public offering.

Unless earlier terminated, this agreement will expire upon the expiration of the last royalty term for a product under the agreement in all countries. The royalty term means, on a product-by-product and country-by-country basis, the period commencing upon the first commercial sale of a product and ending upon the later to occur of: (i) the later of expiration of the last Sigilon patent right that covers the composition of matter, regulatory-approved method of use, or the encapsulation method of a product candidate developed pursuant to the partnership; (ii) 10 years from the date of first commercial sale of such product in such country; or (iii) expiration of any data exclusivity period in such country. Upon the expiration of each royalty term for each product on a country-by-country basis, Lilly's exclusive license will be retained as a fully paid-up, irrevocable and perpetual, exclusive, license with respect to such product in such country. Lilly may terminate this agreement upon prior written notice to us. Each party may terminate this agreement in its entirety upon bankruptcy or similar proceedings of the other party or upon an uncured material breach of the agreement by the other party.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the EU, extensively regulate, among other things, the research, development, testing, manufacturing, packaging, labeling, storage, record keeping, reimbursement, advertising, promotion, distribution, post-approval monitoring and reporting and import and export, pricing and reimbursement of pharmaceutical products, including biological products such as those we are developing. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. Failure to comply with the applicable regulatory requirements at any time during the product development process or post-approval may subject an applicant for marketing approval to delays in development or approval, as well as administrative and judicial sanctions.

License and Regulation of Biologics in the United States

In the United States, our candidate products are regulated by the United States Food and Drug Administration, or the FDA, as biological products, or biologics, under the Public Health Service Act, or the PHSA, and the Federal Food, Drug and Cosmetic Act, or the FDCA, the implementing regulations of the FDA and other federal, state and local statutes and regulations.

An applicant seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps:

- completion of preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency, and purity of the product candidate for each proposed indication, in accordance with current Good Clinical Practices, or GCP;
- preparation and submission to the FDA of a Biologics License Application, or BLA, after completion of all pivotal clinical trials, requesting marketing of the biological product for one or more proposed indications, including submission of detailed information on the manufacture and composition of the product and proposed labelling;
- a determination by the FDA within 60 days of its receipt of a BLA to accept the application for review;
- satisfactory completion of an advisory committee review, if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities, including those of third parties, at which the product, or components thereof, are produced to assess compliance with cGMP requirements; to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity; and, if applicable, the FDA's current good tissue practice, or cGTP, requirements for the use of human cellular and tissue products;
- satisfactory completion of any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCPs and the integrity of clinical data in support of the BLA;
- payment of the application fee under the Prescription Drug User Free Act, or PDUFA, unless exempted; and

- FDA review and approval of the BLA, which may be subject to additional post-approval requirements, including the potential requirement to implement a REMS, and any post-approval studies required by the FDA.

Preclinical Studies and Investigational New Drug Application

Before testing any investigational biological product in humans, including a gene or cell therapy product candidate, the product candidate must undergo preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate the potential for efficacy and toxicity in animals. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including applicable GLP requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application.

An IND is an exemption under the FDCA that allows an unapproved drug or biological product candidate to be shipped in interstate commerce for use in an investigational clinical trial. The central focus of an IND submission is on the general investigational plan and the protocol or protocols for preclinical studies and clinical trials. The IND also includes results of preclinical studies and other evaluations regarding the characteristics of the product, including chemistry, manufacturing and controls information, and any available human data or literature to support the use of the investigational product. The IND is a request for FDA authorization to test the drug or biological product candidate in humans and automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trials can begin. Preclinical or nonclinical testing typically continues even after the IND is submitted.

FDA may, at any time during the initial 30-day IND review period or while clinical trials are ongoing under the IND, impose a partial or complete clinical hold based on concerns for patient safety and/or noncompliance with regulatory requirements. This order issued by the FDA would delay a proposed clinical study or cause suspension of an ongoing study until all outstanding concerns have been adequately addressed, and the FDA has notified the company that investigations may proceed. Imposition of a clinical hold could cause significant delays or difficulties in completing planned clinical studies in a timely manner.

Human Clinical Trials in Support of a BLA

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease to be treated under the supervision of qualified principal investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation.

Clinical trials are conducted under study protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the trial complies with certain FDA regulatory requirements in order to use the trial as support for an IND or application for marketing approval in the United States. Specifically, the FDA requires that such trials be conducted in accordance with GCP requirements, and that FDA must be able to validate the data from such clinical trials through onsite inspections, if FDA deems such inspections necessary.

For clinical trials conducted in the United States, an IND is required, and each clinical trial must be reviewed and approved by an IRB either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, the safety of human

subjects and the possible liability of the institution. An IRB must operate in compliance with FDA regulations. Clinical trials must also comply with extensive GCP rules and the requirements for obtaining subjects' informed consent. The FDA, IRB, or the clinical trial sponsor may suspend or discontinue a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements, including GCP, or the subjects or patients are being exposed to an unacceptable health risk.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group may recommend continuation of the study as planned, changes in study conduct or cessation of the study at designated checkpoints based on access to certain data from the study. Finally, research activities involving infectious agents, hazardous chemicals, recombinant DNA, and genetically altered organisms and agents may be subject to review and approval of an Institutional Biosafety Committee, or IBC, in accordance with NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules. The IBC is 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 the public health or the environment, and such assessment may result in some delay before initiation of a clinical trial.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may be required after approval.

- Phase 1 clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics in healthy humans or, in the case of some products designed to address severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, in patients.

- Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the preliminary efficacy of the product candidate for specific targeted indications and determine dose tolerance and recommended dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.

- Phase 3 clinical trials are undertaken within an expanded patient population at multiple geographically dispersed clinical study sites to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety. A well-controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a biologic; such Phase 3 studies are generally referred to as "pivotal," however, in for some product candidates, Phase 2 may be considered pivotal trials if such trials are expected to provide the clinical evidence needed to support a marketing application.

In some cases, the FDA may approve a BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety or effectiveness after approval. Such post-approval trials are sometimes referred to as Phase 4 confirmatory trials. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and potentially to verify a clinical benefit in the case of biologics approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting required Phase 4 clinical trials could result in withdrawal of approval for products. The FDA generally recommends that sponsors observe subjects for potential gene-therapy related delayed adverse events in a long-term follow-up study of fifteen years for integrating vectors, up to fifteen years for genome editing products and up to five years for AAV vectors. FDA recommends that these long-term follow-up studies include, at a minimum, five years of annual physical examinations followed by annual queries, either in-person or by phone or written questionnaire, for the remaining observation period.

Under the Pediatric Research Equity Act of 2003, or PREA, a BLA or supplement thereto must contain data that are adequate 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. Sponsors must submit a pediatric study plan to FDA outlining the proposed pediatric study or studies they plan to conduct, including study objectives and design, any deferral or waiver requests and other information required by

regulation. The FDA must then review the information submitted, consult with the sponsor and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

For products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with sponsors and FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than 90 days after FDA's receipt of the study plan. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements, under specified circumstances. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Information about certain clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website. Similar requirements for posting clinical trial information in clinical trial registries exist in the EU and in other countries outside the United States.

Marketing Applications for Combination Products

We expect that our product candidates may be subject to regulation as biologic-device combination products. In the United States, products composed of components that would normally be regulated by different centers at FDA are known as combination products. Typically, FDA determines which Center will lead a product's review based upon the product's primary mode of action. Depending on the type of combination product, its approval, clearance or licensure may usually be obtained through the submission of a single marketing application. Regardless of whether our product candidate is considered a biologic-device combination product, we anticipate that our product candidates will be regulated by CBER which will have primary jurisdiction over premarket development and approval. If our product candidates are regulated as biologic-device combination products, FDA may permit a single regulatory submission seeking approval for the product, however, FDA could require separate marketing applications for individual constituent parts of the combination product which may require additional time, effort and information. Even when a single marketing application is required for a combination product, such as a BLA for a combination biologic and device product, both CBER and FDA's Center for Devices and Radiological Health may participate in the review. If a product candidate is considered a biologic-device combination product, an applicant will also need to discuss with the Agency how to apply certain premarket requirements and post-marketing regulatory requirements, including conduct of clinical trials, adverse event reporting and good manufacturing practices, including applicable portions of the FDA's Quality System regulation, to their combination product.

Review and Approval of a BLA

The results of product candidate development, preclinical testing and clinical trials, along with descriptions of the manufacturing process, information on the chemistry and composition of the biological product candidate, proposed labeling and other relevant information are submitted to the FDA as part of a BLA requesting license to market the product. Under federal law, the submission of most BLAs is subject to a substantial application user fee, and the sponsor of an approved BLA is also subject to an annual program fee. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

The FDA has 60 days after submission of the application to conduct an initial review to determine whether it is sufficient to accept for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months for a priority review application. A major amendment to a BLA submitted at any time during the review cycle, including in response to a request from the FDA, may extend the goal date by three months. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs.

During its review of a BLA, the FDA may refer the application to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved and under what conditions. In particular, 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, an advisory committee is a panel of independent experts, including clinicians and other scientific experts. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions about a BLA.

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of non-clinical and clinical trial sites to assure compliance with GCP, the FDA may issue an approval letter or a complete response letter. Under the PHSA, the FDA may approve a BLA if it determines that the product is safe, pure, and potent and that the facility where the product will be manufactured meets standards designed to ensure that it continues to be safe, pure and potent and the approval letter authorizes commercial marketing of the product with specific labeling for specific indications. If the application is not approved, the FDA will issue a complete response letter, which will contain the conditions that must be met in order to secure approval of the application, and when possible will outline recommended actions the sponsor might take to obtain approval of the application. Sponsors that receive a complete response letter may submit to the FDA information that represents a complete response to the issues identified by the FDA. The FDA will not approve an application until issues identified in the complete response letter have been addressed.

If the FDA approves a new product, it may limit the approved indications for use of the product. It may also require that contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require post-approval studies, including Phase 4 clinical trials, to further assess the product's safety or efficacy after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-approval Regulation

Upon FDA approval of a BLA, the sponsor must comply with extensive post-approval regulatory requirements applicable to biological products, including any additional post-approval requirements that the FDA may impose as part of the approval process. These post-approval requirements include, among other things:

- record keeping requirements;
- reporting of certain adverse experiences with the product and production problems to the FDA;
- submission of updated safety and efficacy information to the FDA;
- drug sampling and distribution requirements;
- notifying FDA and gaining its approval of specified manufacturing and labeling changes; and
- compliance with requirements concerning advertising, promotional labeling, industry-sponsored scientific and educational activities and other promotional activities.

Additionally, the sponsor and its third-party manufacturers are subject to periodic unannounced regulatory inspections for compliance with ongoing regulatory requirements, including cGMP and pharmacovigilance regulations.

Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

In addition, the FDA strictly regulates the advertising and labeling of prescription drug products, including biological products. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. Once a drug is approved, the sponsor can make only those claims relating to safety and efficacy, purity and potency that are in accordance with the provisions of the approved label. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us 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 manufacturer's communications on the subject of off-label use of their products. If a company is found to have promoted off-label uses, it may become subject to administrative and judicial enforcement by the FDA, the DOJ, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

After approval, some types of changes to the approved product, such as adding new indications or dosing regimens, manufacturing changes, or additional labeling claims, are subject to further FDA review and approval. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

The FDA may withdraw product 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 issues with manufacturing processes, may result in revisions to the approved labeling to add new safety information, imposition of post-market studies or clinical trials to assess new safety signals or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product recall, seizure, or detention, or refusal to permit the import or export of products; or
- notifying FDA and gaining its approval of specified manufacturing and labeling changes; and
- injunctions or the imposition of civil or criminal penalties.

Orphan Drug Designation

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for the treatment of rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for certain tax credits. In addition, if a drug candidate that has orphan drug designation subsequently receives the first FDA approval for that drug for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years following product approval unless the subsequent product candidate is demonstrated to be clinically superior. Absent a showing of clinical superiority, FDA cannot approve the same product made by another manufacturer for the same indication during the market exclusivity period unless it has the consent of the sponsor or the sponsor is unable to provide sufficient quantities. The concept of what constitutes the "same drug" for purposes of orphan drug exclusivity remains in flux in the context of gene therapies, and in September 2021, the FDA issued final guidance outlining its interpretation of sameness in the context of gene therapy products, and stated it does not intend to consider two gene therapy products to be different drugs based solely on minor differences in the transgenes and/or vectors.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first drug. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation. To qualify for orphan exclusivity, however, the drug must be clinically superior to the previously approved product that is the same drug for the same condition. If a product designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Biosimilars and Exclusivity

The 2010 Patient Protection and Affordable Care Act, or PPACA, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars.

Under the BPCIA, a manufacturer may submit an application for licensure of a biological product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product in any given patient, and (for products administered multiple times to an individual) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. A product shown to be biosimilar or interchangeable with an FDA-approved reference biological product may rely in part on the FDA's previous determination of safety and effectiveness for the reference product for approval, which can potentially reduce the cost and time required to obtain approval to market the product. Complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA. At this juncture, it is also unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was first licensed. This 12-year exclusivity period is referred to as the reference product exclusivity period and bars approval of a biosimilar but notably does not prevent approval of a competing product pursuant to a full BLA (i.e., containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of the product). The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. The law also includes an extensive process for the innovator biologic and biosimilar manufacturer to litigate patent infringement, validity and enforceability prior to the approval of the biosimilar.

There have been ongoing federal legislative and administrative efforts as well as judicial challenges seeking to repeal, modify or invalidate some or all of the provisions of the PPACA. While none of those efforts have focused on changes to the provisions of the PPACA related to the biosimilar regulatory framework, if those efforts continue and if the PPACA is repealed, substantially modified or invalidated, it is unclear what, if any, impact such action would have on biosimilar regulation.

Patent Term Restoration and Extension

A U.S. patent claiming a new biological product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for a single patent for an approved product as compensation for patent term lost during product development and FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date a clinical investigation involving human beings is begun and the submission date of a marketing application less any dime during which the applicant failed to exercise due diligence, plus the time between the submission date of an application and the ultimate approval date less any dime during which the applicant failed to exercise due diligence. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Marketing and Authorization in the EU

To obtain a marketing authorization for a cell or gene therapy product under the EU regulatory system, an applicant must submit an application via the centralized procedure administered by EMA. Specifically, the grant of marketing authorization in the EU for products containing viable human tissues or cells such as cell or gene therapy medicinal products is governed by Regulation 1394/2007/EC on advanced therapy medicinal products, read in combination with Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community code on medicinal products.

Regulation 1394/2007/EC lays down 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's Committee for Advance Therapies which provides a draft opinion regarding the application for marketing authorization and which is subject to final approval as scientific opinion by the EMA's Committee for Medicinal Products for Human Use, or CHMP. The European Commission makes its final decision on whether to grant or refuse the marketing authorization on the basis of the CHMP opinion.

Under the centralized procedure in the EU, the maximum timeframe for the evaluation of a marketing authorization application, or MAA, 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. A request for accelerated assessment may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

Regulatory Data Protection in the EU

In the EU, new active substances approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of marketing exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. This also applies to biosimilars. During the additional two-year period of marketing exclusivity, a generic

marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. In addition if a pediatric investigation plan is accepted and implemented, and an application for a marketing authorization in a pediatric indication is filed, then a product which is eligible for a supplementary protection certificate, or SPC, (similar in effect to a patent term extension) may in some cases benefit from a six-month extension to the term of the SPC. If the product is off-patent and not an orphan, the applicant may benefit from a full period of data and marketing exclusivity (for example, 8+2+1 years) in relation to the pediatric indication. Even if a compound is considered to be a new active substance (chemical or biological) so that the innovator gains the prescribed period of data and marketing exclusivity, another company may market another version of the same medicinal product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the EU market (in the case of the centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid. The same rules apply in the United Kingdom following Brexit.

Regulatory Requirements After Marketing Authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include compliance with the EU's and the United Kingdom’s stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of authorized products must also be conducted in strict compliance with the EU's cGMP requirements, which mandate the methods, facilities, and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. The EU has also drawn up guidelines which develop the cGMP requirements that should be applied in the manufacturing of advanced therapy medicinal products, which would apply to cell and gene therapy products. The United Kingdom is continuing to apply the same regulations as the EU with respect to cGMP requirements. The marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU under Directive 2001/83EC, as amended, and through national legislation of the EU member states.

Clinical Trial Approval

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on GCP, a system for the approval of clinical trials in the EU has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of each EU member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after ethical approval covering that site has been obtained in accordance with the applicable national legislation. In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC six months after the new clinical trial portal is announced by the European Commission to be ready for use. This new legislation, which will be directly applicable in all member states, aims at simplifying and streamlining the approval of clinical trials in the EU by allowing for a streamlined application procedure via a single-entry point and strictly defined deadlines for the assessment of clinical trial applications.

Conditional Marketing Authorization

For medicinal products where the benefit of immediate availability outweighs the risk of less comprehensive data than normally required, based on the scope and criteria defined in legislation and guidelines, it is possible to obtain from the EMA a conditional marketing authorization with a 12-month validity period and annual renewal pursuant to Regulation No 507/2006. These are granted only if the CHMP finds that all four of the following requirements are met: (i) the benefit-risk balance of the product is positive; (ii) it is likely that the applicant will be able to provide comprehensive data; (iii) unmet medical needs will be fulfilled; and (iv) the benefit to public health of the medicinal product's immediate availability on the market outweighs the risks due to need for further data.

PRIME Designation in the EU

The EMA has a Priority Medicines, or PRIME, scheme for products falling within the remit of the centralized authorization procedure. The PRIME scheme is intended to encourage drug development in areas of unmet medical need and may provide accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, the potential for frequent discussions on clinical trial designs and other development program elements, and an expectation of accelerated assessment once a dossier has been submitted.

Orphan Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicine by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition. If an orphan designation is obtained, the product will generally benefit from ten years of market exclusivity (extended by two further years for products which have also complied with an agreed pediatric investigation plan granted at the time of the orphan medicine designation). Market exclusivity means that similar medicines for the same indication generally cannot be placed on the market during the exclusivity period unless the relevant applicant can establish that its medicinal product is safer, more effective or otherwise clinically superior. The United Kingdom intends to offer similar incentive schemes for orphan drugs.

General Data Protection Regulation

The collection, use, disclosure, transfer or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area, or the EEA, and the processing of personal data that takes place in the EEA, is subject to the EU's General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, and it imposes heightened requirements on companies that process health and other sensitive data, such as requiring in many situations that a company obtain the consent of the individuals to whom the sensitive personal data relate before processing such data. Examples of obligations imposed by the GDPR on companies processing personal data that fall within the scope of the GDPR include providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, appointing a data protection officer, providing notification of data breaches and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance. The United Kingdom and the EU are currently accepting that the privacy regimes of each country are equivalent so that personal might be transferred between those jurisdictions without additional requirements.

Coverage, Pricing, and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may seek regulatory approval by the FDA or other government authorities. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use any product candidates we may develop unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such product candidates. Sales of our products will depend, in part, on the availability of coverage and the adequacy of reimbursement from third-party payors.

Within the United States, third-party payors include government authorities or government healthcare programs, such as Medicare and Medicaid, and private entities, such as managed care organizations, private 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 reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Some third-party payors may manage utilization of a particular product by requiring pre-approval (known as "prior authorization") for coverage of particular prescriptions (to allow the payor to assess medical necessity).

Moreover, a third-party payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain net price levels sufficient to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for drug products can differ significantly from payor to payor. One third-party payor's decision to cover a particular drug product or service does not ensure that other payors will also provide coverage for the drug product, or will provide coverage at an adequate reimbursement rate.

Third-party payors are increasingly challenging the price and examining the cost-effectiveness of new products and services in addition to their safety and efficacy. To obtain or maintain coverage and reimbursement for any current or future product, we may need to conduct expensive pharmacoeconomic studies to demonstrate the medical necessity and cost-effectiveness of our product. These studies will be in addition to the studies required to obtain regulatory approvals. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to

allow a company to sell its products at a profit. Thus, obtaining and maintaining reimbursement status is time-consuming and costly.

As noted above, 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 coverage and adequate reimbursement. There is an emphasis on cost containment measures in the United States and we expect will continue to increase the pressure on pharmaceutical pricing. 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 product candidates for which we receive regulatory approval from one or more third party payors, less favorable coverage policies and reimbursement rates may be implemented in the future.

If we obtain appropriate approval in the future to market any of our current product candidates in the United States, we may be required to provide discounts or rebates under government healthcare programs or to certain government and private purchasers in order to obtain coverage under federal healthcare programs such as Medicaid. Participation in such programs may require us to track and report certain drug prices. We may be subject to fines and other penalties if we fail to report such prices accurately. More generally, we may need to provide price concessions to third party payors to obtain favorable coverage or to purchasers to achieve sales. Arrangements with third party payors or purchasers may include value-based arrangements under which the amount paid for products depends on the performance of the product.

Outside the United States, ensuring adequate coverage and payment for any product candidates we may develop will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of any product candidates we may develop to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the EU, pricing and reimbursement schemes vary widely from country to country because this is not yet the subject of harmonized EU law. Many countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies (so-called health technology assessments) in order to obtain reimbursement or pricing approval and others with "peg" their pricing to a basket of other countries. EU member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market, both are possible in the United Kingdom. Some member states, in addition to controlling pricing will monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. 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, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of pharmaceutical products that are granted marketing approval. Our arrangements with providers, third-party payors, and other customers and our operations generally, are subject to broadly applicable fraud and abuse, FDA, and data privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Federal and state healthcare laws and regulations, some of which would apply if and when we have a marketed product, include the following:

- federal false claims, false statements and civil monetary penalties laws prohibiting, among other things, any person from knowingly presenting, or causing to be presented, a false claim for payment of government funds or knowingly making, or causing to be made, a false statement to get a false claim paid;

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual for, or the purchasing or ordering of, a good or service for which payment may be made under federal healthcare programs such as Medicare and Medicaid;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which, in addition to privacy protections applicable to healthcare providers and other entities, prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- the federal Food, Drug, and Cosmetic Act, or the FDCA, which among other things, strictly regulates drug marketing, prohibits manufacturers from marketing such products for off-label use and regulates the distribution of samples;

- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs;

- the so-called "federal sunshine" law, which requires pharmaceutical and medical device companies to monitor and report certain financial interactions with certain healthcare providers as well as ownership and investment interests held by physicians and their immediate family members to the Centers for Medicare & Medicaid Services within the U.S. Department of Health and Human Services for re-disclosure to the public;

- analogous state and foreign laws and regulations, such as state anti-bribery, anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with specific compliance standards, restrict financial interactions between pharmaceutical companies and healthcare providers or require pharmaceutical companies to report information related to payments to health care providers or marketing expenditures. Other state laws may require pharmaceutical companies to file reports relating to pricing and marketing information, and state and local laws may require registration of pharmaceutical sales representatives.

Healthcare and Other Reform

In the United States, there have been and continue to be a number of significant legislative initiatives to contain healthcare costs. Federal and state governments continue to propose and pass legislation designed to reform delivery of, or payment for, health care, which include initiatives to reduce the cost of healthcare. For example, in March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act, as amended, the Health Care and Education Reconciliation Act, or the Affordable Care Act, which, among other things, expanded health care coverage through Medicaid expansion and the implementation of the individual mandate for health insurance coverage and which included a number of changes to the coverage and reimbursement of drug products under government healthcare programs.

Beyond the Affordable Care Act, there have been ongoing health care reform efforts. Drug pricing and payment reform was a focus of the Trump Administration and has been a focus of the Biden Administration. For example, federal legislation enacted in 2021 eliminates a statutory cap on Medicaid drug rebate program rebates effective January 1, 2024. As another example, the Inflation Reduction Act (“IRA”) of 2022 includes a number of changes intended to address rising prescription drug prices in Medicare Parts B and D. These changes, which have varying implementation dates, include caps on Medicare Part D out-of-pocket costs, Medicare Part B and Part D drug price inflation rebates, a new Medicare

Part D manufacturer discount drug program and a drug price negotiation program for certain high spend Medicare Part B and D drugs.

Healthcare reform efforts have been and may continue to be subject to scrutiny and legal challenge. For example, with respect to the Affordable Care Act, tax reform legislation was enacted that eliminated the tax penalty established for individuals who do not maintain mandated health insurance coverage beginning in 2019 and, in 2021, the U.S. Supreme Court dismissed the latest judicial challenge to the Affordable Care Act brought by several states without specifically ruling on the constitutionality of the Affordable Care Act. As another example, revisions to regulations under the federal anti-kickback statute would remove protection for traditional Medicare Part D discounts offered by pharmaceutical manufacturers to pharmacy benefit managers and health plans. Pursuant to court order, the removal was delayed and recent legislation imposed a moratorium on implementation of the rule until January 2032.

There have also been efforts by federal and state government officials or legislators to implement measures to regulate prices or payment for pharmaceutical products, including legislation on drug importation. Recently, there has been considerable public and government scrutiny of pharmaceutical pricing and proposals to address the perceived high cost of pharmaceuticals. There have also been recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices.

General legislative cost control measures may also affect reimbursement for our product candidates. The Budget Control Act, as amended, resulted in the imposition of reductions in Medicare (but not Medicaid) payments to providers in 2013 and will remain in effect through 2031 (except May 1, 2020 to March 31, 2022) unless additional Congressional action is taken. Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented and/or any significant taxes or fees that may be imposed on us could have an adverse impact on our results of operations.

Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our current or future products if approved for sale. We cannot, however, predict the ultimate content, timing or effect of any changes to the Affordable Care Act or other federal and state reform efforts. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results.

Human Capital

Employees

As of December 31, 2022, following our strategic reprioritization, we had 62 full-time permanent employees. Of these employees, 15 have an M.D. or a Ph.D. Ten of our employees work in administration and operations and 52 work in research and development. None of our employees are represented by a labor union or covered by collective bargaining agreements, and we believe our relationship with our employees is good.

Talent Acquisition and Development

We consider the intellectual capital, skills and experience of our employees to be an essential driver of our business and key to our future prospects. We face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions, and we believe that our future success will depend in large part on our continued ability to attract and retain highly skilled employees. To attract qualified applicants to our company and retain our employees, we offer a competitive total rewards package consisting of base salary and cash target bonus a comprehensive benefit package and equity compensation for every employee. Annual cash bonus opportunity and equity compensation increase as a percentage of total compensation based on level of responsibility. Any actual bonus payout is based on a combination of individual performance and corporate performance.

Diversity, Inclusion, and Belonging

We value diversity at all levels of the organization and continue to focus on extending our diversity, equity and inclusion initiatives across our entire workforce, from: working with managers to develop strategies for building diverse,

high performing teams; to ensuring that we attract, develop and retain diverse talent from all backgrounds; to increasing awareness within our company of unconscious biases, and supporting individuals who are underrepresented in our company, industry or society, such as women, members of the LGBTQ community and people of color. In addition, we pride ourselves on an open culture that respects co-workers, values employees' health and well-being and fosters professional development. We support employee growth and development in a variety of ways including with group training and individual mentoring and coaching. Our management routinely reports to our board of directors on human capital management topics, including corporate culture, diversity, equity and inclusion, employee development and retention, and compensation and benefits. Similarly, our board of directors regularly provides input on important decisions relating to these matters, including with respect to employee compensation and benefits, talent retention and development.

Company Founding

We were founded in 2015 by Flagship Pioneering, working together with academic co-founders Drs. Robert Langer and Daniel Anderson of MIT, to develop and commercialize a new category of therapeutics to treat human diseases. Our platform technology was inspired by a decade of work at MIT demonstrating, in principle, that capsules made of novel engineered biomaterials, which do not trigger a foreign body response (or scarring), could be implanted in animals for extended periods and support the survival of cells producing a therapeutic protein without the need for immunosuppression. A Flagship Labs innovation team at Flagship Pioneering, led by Managing Partner Dr. Douglas Cole, M.D., our founding and current Chairman, and, subsequently, Sigilon's research and development team, built on this seminal work to expand and scale this approach and show its potential to address a range of unmet needs in multiple therapeutic areas. Since our formation, we have established a highly collaborative, patient first culture that drives our passion for innovation. Our management team has extensive expertise in chronic diseases, human genetics and cell and gene engineering. We are led by Dr. Rogerio Vivaldi Coelho, our President and Chief Executive Officer, who has more than 30 years of experience as a physician and as an industry executive. Prior to joining Sigilon, Dr. Vivaldi served as Executive Vice President and Chief Global Therapeutics Officer at Bioverativ Inc. from 2016 until it was acquired by Sanofi S.A. in 2018, and served as Chief Commercial Officer at Spark Therapeutics, Inc. between 2014 and 2016. Before that, he led Genzyme's rare disease business as President of both the rare disease business and the renal & endocrine group, as well as Senior Vice President and General Manager of Genzyme's Latin America Group during his 20 year tenure at Genzyme.

Legal proceedings

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business.

Our Corporate Information

We were incorporated in Delaware in May 2015 under the name VL36, Inc. and commenced operations in February 2016, when we changed our name to Sigilon, Inc. In June 2017, we changed our name to Sigilon Therapeutics, Inc. Our principal executive offices are located at 100 Binney Street, Suite 600, Cambridge, MA 02142, and our telephone number is (617) 336-7540. Our website is www.sigilon.com. Information contained on, or that can be accessed through, our website is not part of this Annual Report on Form 10-K.

Our website is www.sigilon.com, and our investor relations website is located at ir.sigilon.com. We make available on or through our website certain reports and amendments to those reports that we file with or furnish to the SEC in accordance with the Securities Exchange Act of 1934, as amended. These include our annual reports on Form 10-K, our quarterly reports on Form 10-Q, and our current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC. The information contained or incorporated on our website is not a part of this Annual Report on Form 10-K.

The SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding us and other issuers that file electronically with the SEC. The SEC's Internet website address is http://www.sec.gov.

Item 1A. Risk Factors

You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report on Form 10-K. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

We are currently advancing our pipeline of programs in development. Discovering development candidates and developing investigational therapeutics is expensive, and we expect to continue to spend substantial amounts to (i) perform basic research, perform preclinical studies, and conduct clinical trials of our current and future programs, (ii) continue to develop and expand our Shielded Living Therapeutics, or SLTx, platform and infrastructure and supply preclinical studies and clinical trials with appropriate grade materials, including cGMP materials, (iii) seek regulatory approvals for our product candidates, and (iv) launch and commercialize any product candidates for which we receive regulatory approval.

Since inception, we have incurred significant operating losses. Our net loss was $43.6 million and $77.3 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $256.8 million. We have financed our operations primarily through the sale of equity securities, payments received under our collaboration agreement and proceeds from borrowings under our credit facilities. We have devoted all of our efforts to research and development. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- continue our current research programs and our preclinical development of product candidates from our current research programs;
- seek to identify additional research programs and additional product candidates;
- conduct additional preclinical studies for our product candidates;
- initiate clinical trials for our Mucopolysaccharidosis Type I, or MPS-1, program, or any other product candidates;
- comply with regulatory requirements established by the FDA, the European Medicines Agency, or EMA, and other comparable foreign regulatory authorities;
- seek marketing approvals for any of our product candidates;
- ultimately establish a sales, marketing, and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval;
- further develop our SLTx platform;
- hire additional research, development, manufacturing, quality, supply chain and commercial personnel;
- continue to hire and retain research and clinical personnel;

- add operational, financial, corporate development and management information systems and legal personnel, including personnel to support our product development and planned future commercialization efforts;

- expand our facilities;

- acquire or in-license product candidates, intellectual property and technologies;

- scale up manufacturing and supply chain capacity to meet future clinical and commercial demand, including scaling up processes for cell culture and automated encapsulation, and building or expanding our manufacturing capabilities or capacity, including future manufacturing facilities;

- file, prosecute, defend, and enforce our patent claims and other intellectual property rights, including patent infringement actions brought by third parties against us regarding our investigational medicines or actions by us challenging the patent or intellectual property rights of others, and provide reimbursement of third-party expenses related to our patent portfolio; and

- operate as a public company.

We are currently in the preclinical testing stages for all of our research programs. We expect that it will be many years, if ever, before we have a product candidate ready for commercialization. To become and remain profitable, we must, either directly or through collaborators, develop and eventually commercialize a medicine or medicines with significant market potential. This will require us to be successful in a range of challenging activities, including identifying product candidates, completing preclinical testing and clinical trials of product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing, and selling those medicines for which we may obtain marketing approval, and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. Because of the numerous risks and uncertainties associated with developing product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all. 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 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 could also cause you to lose all or part of your investment.

If we cannot comply with Nasdaq's continued listing standards, our common stock could be delisted, which would harm our business, the trading price of our common stock, our ability to raise additional capital and the liquidity of the market for our common stock.

Our common stock is currently listed on The Nasdaq Global Select Market. To maintain the listing of our common stock on The Nasdaq Global Select Market, we are required to meet certain listing requirements, including related to the price of our common stock. As previously disclosed, on June 22, 2022, we received a written notice, or Notice, from the Listing Qualifications Department of The Nasdaq Stock Market, or Nasdaq, notifying us that we no longer complied with the minimum bid price requirement of $1.00 for continued listing on The Nasdaq Global Select Market. On December 20, 2022, we received notice from Nasdaq indicating that Nasdaq had determined to delist our securities from The Nasdaq Global Select Market based upon our continued non-compliance with the $1.00 bid price requirement. Subsequently, we participated in a hearing before the Nasdaq Hearings Panel on February 9, 2023, after which we were granted a stay of delisting procedures subject to our meeting certain conditions, including an agreement to effect a reverse stock split. However, there can be no assurance that a reverse stock split would be approved by our stockholders or would result in a sustained higher stock price that would allow us to meet the Nasdaq stock price listing requirements. If our common stock were delisted, we could seek to list our common stock on The Nasdaq Capital Market or trade our common stock on the OTC Markets. Listing on such other market or exchange could reduce the liquidity of our common stock and impede our ability to raise capital.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce, reprioritize, or eliminate our research and product development programs or future commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate clinical trials of, and seek marketing approval for product candidates. We expect that our cash, cash equivalents and marketable securities as of December 31, 2022 of $69.6 million would enable us to fund our operating expenses, capital expenditures requirements and debt service payments into 2025. If we obtain marketing approval for any product candidate, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, manufacturing, and distribution are not the responsibility of a collaborator. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations, including operating as a public company. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, reprioritize, or eliminate our research and product development programs or future commercialization efforts.

Our operating plan may change as a result of factors currently unknown to us, and we may need to seek funding sooner than planned. Our future capital requirements will depend on many factors, including:

- the costs of continuing to develop our SLTx platform;
- the costs of acquiring licenses for the components of our products and engineered cell lines that will be used with our current and future product candidates;
- the scope, progress, results, and costs of discovery, preclinical development, formulation development, and clinical trials for our current and future product candidates;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims;
- the costs, timing, and outcome of regulatory reviews associated with our product candidates;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, distribution, coverage and reimbursement for our program in MPS-1 or any other product candidates for which we receive regulatory approval;
- the cost of developing and expanding our manufacturing capabilities and advancing these manufacturing capabilities to manufacture product candidates that are commercially viable;
- additional expenses attributable to inflation and related impacts on our supplies of raw materials for our product candidates;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the success of any collaborations that we may establish and of our license agreements;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain; and
- the extent to which we acquire or in-license product candidates, intellectual property and technologies.

Identifying 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, even if we successfully identify and develop product candidates and those are approved, we may not achieve commercial success. Our commercial revenues, if any,

will be derived from sales of medicines 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.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Disruptions in the financial markets could make equity and debt financing more difficult to obtain and may have a material adverse effect on our ability to meet our fundraising needs. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Our license agreements and any future collaboration agreements may also be terminated if we are unable to meet the payment or other obligations under the agreements. We could be required to seek collaborators for our product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to our product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates we may develop.

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, including through our at-the-market, or ATM, equity offering program, debt financings, collaborations, strategic alliances, and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Additional debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends, and possibly other restrictions.

If we raise funds through additional 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 we may develop, or we may have to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are an early-stage company. We were founded in 2015 and commenced operations in 2016. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our SLTx platform, identifying product candidates, undertaking preclinical studies and initiating a clinical study for one product candidate, for which we deprioritized in December 2021 following a clinical hold and for which we withdrew the IND and CTA. We expect to complete close out activities for this study in the first half of 2023. All of our product candidates are in the research or preclinical stage and the risk of failure for our programs is high. We have not yet demonstrated an ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about 10 to 15 years to develop a product candidate from the time it is discovered to when it is available for treating patients, if ever.

Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Our limited operating history may make it difficult to evaluate our technologies and industry and predict our future performance. Our short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

We have never generated revenue from product sales and may never become profitable.

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaborative partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize our current and future product candidates. We do not anticipate generating revenues from product sales for the next several years, if ever. Our ability to generate future revenues from product sales depends heavily on our, or our collaborators', ability to successfully:

- complete research and preclinical and clinical development of our current and future product candidates;
- continue to develop new product candidates;
- seek and obtain regulatory and marketing approvals for any of our product candidates for which we complete clinical trials;
- launch and commercialize any of our product candidates for which we obtain regulatory and marketing approval by establishing a sales force, marketing, and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- qualify for coverage and establish adequate reimbursement by government and third-party payors for any of our product candidates for which we obtain regulatory and marketing approval;
- develop, maintain, and enhance a sustainable, scalable, reproducible, and transferable manufacturing process for the product candidates we may develop;
- establish and maintain supply and manufacturing capabilities or capacities internally or with third parties that can provide adequate, in both amount and quality, products, and services to support clinical development and the market demand for any of our product candidates for which we obtain regulatory and marketing approval;
- obtain market acceptance of current or any future product candidates as viable treatment options;
- address competing technological and market developments;
- implement internal systems and infrastructure, as needed;
- negotiate favorable terms in any collaboration, licensing, or other arrangements into which we may enter and performing our obligations in such collaborations;
- maintain, protect, enforce, defend, and expand our portfolio of intellectual property rights, including patents, trade secrets, and know-how;
- avoid and defend against third-party interference, infringement, and other intellectual property claims; and
- attract, hire, and retain qualified personnel.

Even if one or more of our current and future product candidates are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA or the EMA, or other regulatory authorities to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved product candidates, we may not become profitable and may need to obtain additional funding to continue operations.

The transition away from LIBOR may adversely affect our cost to obtain financing.

On July 27, 2017, the U.K. Financial Conduct Authority announced that it would stop persuading or compelling banks to submit London Interbank Offered Rate, or LIBOR, rates after 2021. The Financial Conduct Authority and the ICE Benchmark Administration announced that LIBOR may continue for legacy contracts until June 2023. The Alternative Reference Rates Committee, a steering committee comprised of United States financial market participants, selected and the Federal Reserve Bank of New York, has recommended the Secured Overnight Finance Rate, or SOFR, as an alternative to LIBOR. SOFR is a broad measure of the cost of borrowing cash in the overnight United States treasury repo market. There can be no assurance that rates linked to SOFR or associated changes related to the adoption of SOFR will be as favorable to us as LIBOR and may result in an effective increase in the applicable interest rate on our current or future debt obligations, including our 2020 Credit Facility.

Risks Related to Preclinical and Clinical Development of Our Technologies

Negative results of preclinical or clinical studies of any of our product candidates may require us to discontinue or delay development of other product candidates, which are all based on the same SLTx platform.

Since all of the product candidates in our current pipeline are based on the same SLTx platform, if the results of our research and development activities reveal any underlying problem with our SLTx platform, then we may be required to make changes to our platform, which may be difficult to implement or complete, or to discontinue development of all of our product candidates, which would cause our portfolio of product candidates to have little value. For example, in November 2021, we reported that spheres covered with PFO were observed during a retrieval procedure in our Phase 1/2 study of SIG-001. Our remaining product candidates have been developed using the same SLTx platform that supported the development of SIG-001 and we may therefore encounter similar challenges in development of other product candidates developed using this platform.

Further, the FDA or other regulatory authorities may not allow us to pursue further development of any of our product candidates as a result of the issues presented by the serious adverse event reported in our Phase 1/2 clinical trial of SIG-001 or our finding of PFO, particularly if we are unable to demonstrate an acceptable risk-benefit profile for product candidates developed using our SLTx platform. If the FDA or other regulatory agencies express safety, tolerability or efficacy concerns, additional preclinical studies or clinical trials involving our current product candidates, amendments to the enrollment criteria and/or clinical trial protocols for our future studies or changes to our platform, including our cells, spheres or manufacturing processes, may be needed and may be difficult to implement or complete. In such cases, our progress in the development of a product candidate for MPS-1 and other product candidates may be significantly slowed or stopped and the associated costs may be significantly increased, adversely affecting our business.

The SLTx platform consists of novel technologies that are not yet clinically validated for human therapeutic use. The regulatory requirements applicable to our product candidates may change over time. The approaches we are taking to discover and develop novel therapeutics are unproven and may never lead to marketable products.

The regulatory approval process for novel cellular therapy product candidates such as ours is unclear and may be lengthier and more expensive than the process for other, better-known or more extensively studied product candidates, such as biologics, small molecule drugs and other more traditional pharmaceuticals.

Regulatory requirements governing cell therapy products have changed and may continue to change in the future. The FDA has established the Office of Therapeutic Products, or OTP, within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of cell therapy and related products, and has established the Cellular, Tissue

and Gene Therapies Advisory Committee to advise CBER in its review. Our product candidates have not been reviewed by OTP to date, but this could change if the FDA changes any of its guidance or regulations. If we were to engage an NIH-funded institution to conduct a clinical trial, that institution's biosafety committee, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules, as well as its institutional review board, or IRB, would need to review the proposed clinical trial to assess the safety of the trial. Similarly, the EMA may issue new guidelines concerning the development and marketing authorization for cell therapy medicinal products and require that we comply with these new guidelines.

Regulatory review committees and advisory groups, and any new guidelines they promulgate, may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our current or future product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a product to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects would be harmed. Even if our product candidates are approved, we expect that the FDA will require us to submit follow-up data regarding our clinical trial subjects for a number of years after any approval. If this follow-up data shows negative long-term safety or efficacy outcomes for these patients, the FDA may revoke its approval or change the label of our products in a manner that could have an adverse impact on our business.

In addition, adverse developments in clinical trials of cell therapy products conducted by others or regulatory review of the serious adverse event that occurred in our Phase 1/2 clinical trial of SIG-001 or the finding of PFO, may cause the FDA or other oversight bodies to change the requirements for approval of any of our other product candidates. As a result, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates.

We may not be successful in our efforts to identify and develop product candidates. If these efforts are unsuccessful, we may never become a commercial stage company or generate any revenues.

The success of our business depends primarily upon our ability to identify, develop, and commercialize product candidates using on our SLTx platform. Because all of our remaining programs are in the research or preclinical stage, we have not yet been able to definitively assess the safety, tolerability or efficacy of our product candidates in humans, and there may be effects from treatment with any of our current or future product candidates that we cannot predict at this time.

We are implementing potential platform optimizations, including changes to our cells, spheres and manufacturing processes to address findings of PFO in our Phase 1/2 clinical trial of SIG-001. We may determine that additional changes to our platform are needed that may be difficult, costly, or time consuming to implement or complete.

Additionally, our research programs may fail to identify product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying product candidates, our product candidates may be shown to have harmful side effects in preclinical *in vitro* experiments or animal model studies, they may not show promising signals of therapeutic effect in such experiments or studies or they may have other characteristics that may make the product candidates impractical to manufacture or dose, unmarketable, or unlikely to receive marketing approval. If any of these events occur, we may be forced to abandon our research or development efforts for a program or programs, which would have a material adverse effect on our business, financial condition, results of operations, and prospects.

We are early in our development efforts. It will be many years before we or our collaborators commercialize a product candidate, if ever. If we are unable to advance our product candidates to clinical development, obtain regulatory

approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts and have focused our research and development efforts to date on select indications, including endocrine diseases, lysosomal diseases and other acute and chronic disorders, when identifying our initial targeted disease indications and our initial product candidates. We expect to conduct IND-enabling studies for SIG-002 and other product candidates, but there is no guarantee that the results from such IND-enabling studies will enable us to commence clinical trials of our product candidates in a timely manner, or at all.

We have not submitted INDs to the FDA or similar filings to any other regulatory agency for any of our current product candidates. We have invested substantially all of our efforts and financial resources in building our SLTx platform, and the identification and preclinical development of our current product candidates. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We currently generate no revenue from sales of any product and we may never be able to develop or commercialize a marketable product.

Commercialization of our product candidates will require additional preclinical and clinical development; regulatory and marketing approval in multiple jurisdictions, including by the FDA and the EMA; obtaining manufacturing supply, capacity and expertise; building of a commercial organization; and significant marketing efforts. The success of our current and future product candidates will depend on many additional factors, including the following:

- successful completion of preclinical studies resulting in data that is supportive of advancing to an IND or CTA submission;
- successful submissions of INDs or comparable foreign applications that allow commencement of our clinical trials, including resolving any clinical holds that may be imposed on such submissions;
- successful initiation, enrollment in, and completion of, clinical trials;
- positive results from clinical trials that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended populations;
- receipt of marketing approvals from applicable regulatory authorities;
- successful development of manufacturing processes and transfer to cGMP facilities of appropriate scale for clinical supply;
- successful validation of manufacturing processes at the cGMP facilities for commercial supply;
- establishment of cGMP manufacturing capability either by contracting third party manufacturers, or CMO, or by building our own manufacturing facility;
- obtaining and maintaining patent, trade secret, and other intellectual property protection and non-patent exclusivity for our product candidates;
- launching commercial sales of the product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the products, if and when approved, by patients, the medical community, and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile of the product candidates following approval;

- enforcing and defending intellectual property and proprietary rights and claims; and

- supplying the products at a price that is acceptable to the pricing or reimbursement authorities in different countries, and at a cost that is profitable.

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

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications among many potential options. 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. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities or we may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful, which would be costly and time consuming. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. 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. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Drug development is a lengthy, expensive, and inherently uncertain process, with a high risk of failure at every stage of development, and any favorable preclinical results are not predictive of results that may be observed in clinical trials.

Drug development is a highly uncertain process, and failure can occur at any stage of development. There is a high rate of attrition for product candidates in preclinical and clinical trials due to scientific feasibility, safety, efficacy, changing standards of medical care and other variables. The risk of failure is heightened for product candidates that are based on new technologies, such as our SLTx platform. Data obtained from preclinical and clinical activities are subject to varying interpretations and analyses, which may delay, limit or prevent regulatory approval. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical development have nonetheless failed to obtain marketing approval of their product candidates. As we generate preclinical results, such results will not ensure that later preclinical studies or clinical trials will demonstrate similar results.

We have not yet initiated clinical trials for any product candidate other than SIG-001, for which we expect to complete close out activities in the first quarter of 2023.

There is a high failure rate for drugs and biologics proceeding through preclinical studies and clinical trials. Our prioritized programs for MPS-1 and diabetes and other product candidates may fail to demonstrate sufficient safety and efficacy levels. In addition, even if initial clinical trials in any of our current or future product candidates are successful, these product candidates may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through preclinical studies and initial clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials.

In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development and clinical holds that may be imposed on our clinical trials. Any such adverse events may cause us to delay, limit, or terminate our clinical trials, any of which would have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our product candidates are composed of engineered human cell lines, encapsulated in a biocompatible matrix sphere. To date, there have been no completed human clinical trials for product candidates arising from our SLTx platform or consisting of our cell or sphere technologies. There may be serious adverse events, undesirable side effects related to either component of our product candidates, or limited efficacy of product candidates arising from our SLTx platform.

If any other product candidates we develop, in addition to SIG-001, are associated with serious adverse events, undesirable side effects, unexpected characteristics or limited efficacy or if the risk-benefit profile of such products is adversely impacted, we may need to abandon or modify their development or limit development to certain uses or subpopulations in which the serious adverse events, undesirable side effects, other characteristics or limited efficacy are less prevalent, less severe, or more acceptable from a risk-benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations, and prospects. For example, if our future preclinical and clinical studies of our product candidates result in additional incidences of PFO, we may be unable to support an appropriate risk-benefit profile of our product candidates. Many product candidates that initially showed promise in early-stage testing for endocrine, lysosomal diseases and other acute and chronic disorders have later been found to cause side effects that prevented further clinical development of the product candidates.

If our clinical trials result in a high and unacceptable severity and/or prevalence of adverse events or limited efficacy due to the formation of inhibitors or PFO or other characteristics, the FDA, the EMA or other regulatory authorities could require us to cease further development of, or deny approval of, any product candidates we are able to develop for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events or incidences of PFO are not product related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate we may develop, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to identify and develop product candidates, and may harm our business, financial condition, result of operations, and prospects significantly.

Additionally, if we successfully develop a product candidate and it receives marketing approval, 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 outweighs the risks for each potential patient, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive, and more costly than what is typical for the industry. Furthermore, if we or others later identify undesirable side effects caused by any product candidate that we develop, if the results of our clinical trials or tests are not positive or are only modestly positive or if there are safety concerns, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate, or may refuse to approve supplemental applications for such product candidate;
- regulatory authorities may require additional warnings on the label, such as a “Boxed Warning” or contraindication, or limit the approved use of such product candidate;
- regulatory authorities may impose additional restrictions on the marketing of, or the manufacturing processes for, the particular product candidate;
- we may be required to recall the product or change the way it is administered in patients;
- we may be required to conduct additional clinical trials;
- we may lose the support of collaborators, requiring us to bear more of the costs associated with research and development;
- we may only obtain approval for indications or patient populations that are not as broad as intended or desired;

- we may only obtain marketing approval in some countries but not others;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our current and future product candidates and could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If clinical trials of our current and future product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of any of our current and future product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results.

We and our collaborators have and may continue to experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to complete such clinical trials, receive marketing approval or commercialize our current and future product candidates, including:

- delays in reaching a consensus with regulators on trial design;
- regulators, IRBs, or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delays in reaching or failing to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective contract research organizations, or 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;
- difficulties in recruiting investigators of appropriate competence and experience for our clinical trials;
- the number of patients required for clinical trials of any of our current and future product candidates may be larger than we anticipate; enrollment of suitable participants in these clinical trials may be delayed or slower than we anticipate; or patients may drop out of these clinical trials 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;
- regulators, IRBs, or independent ethics committees may impose a clinical hold and require that we or our investigators suspend or terminate clinical research or clinical trials of any of our current and future product candidates for various reasons;
- noncompliance with regulatory requirements, a finding of undesirable side effects or other unexpected characteristics, or that the participants are being exposed to unacceptable health risks or after an inspection of our clinical trial operations or trial sites;
- failure to perform clinical trials in accordance with study protocols, Good Clinical Practice, or GCP, requirements, and other regulatory requirements;

- the cost of clinical trials of any of our current and future product candidates may be greater than we anticipate;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- delays in participation in a trial as a result of failure to deliver treatment doses to clinical trial sites in a timely manner, the logistical burden of dose delivery or failure by clinical trial sites to store treatment doses according to protocols;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- occurrence of new or recurring serious adverse events associated with any of our current and future product candidates that are viewed to outweigh their potential benefits, and related clinical holds;
- occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors;
- the supply or quality of any of our current and future product candidates or other materials necessary to conduct clinical trials of any of our current and future product candidates may be insufficient or inadequate, including as a result of delays in the manufacturing, testing, and delivery of any of our current and future product candidates to the clinical sites by us or by third parties with whom we have contracted to perform certain of those functions;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; and
- clinical trials of any of our current and future product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development or research programs altogether.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination 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 or sufficient benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend any future clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Product development costs will also increase if we or our collaborators experience delays in clinical trials or other testing or in obtaining marketing approvals. We do not know whether our clinical trials will begin as planned, 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 any product candidates we may develop, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize any product candidates we may develop, any of which may harm our business, financial condition, results of operations, and prospects.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required

to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in review, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of our product candidates.

If we experience delays or difficulties in the enrollment and dosing of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Identifying and qualifying patients to participate in clinical trials for our product candidates is critical to our success. The timing of our clinical trials will depend on our ability to recruit patients to participate in our studies as well as the dosing of such patients and completion of required follow-up periods. There are also a number of other product candidates in development by our competitors, who compete for the same limited patient populations. If we or our collaborators are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, the EMA or other analogous regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial, we may not be able to initiate clinical trials for our current and future product candidates. Enrollment may be particularly challenging for some of the rare diseases we are targeting in our most advanced programs. For example, the approximate incidence of MPS-1 is one in 100,000 live births and only approximately 4,000 to 5,000 patients with Fabry disease are known in the United States. In addition, the number of patients eligible to enroll in our clinical trials may turn out to be lower than expected if certain patient populations such as pediatric subpopulations are not eligible to participate in our clinical trials.

If patients are unwilling to participate in our studies because of negative publicity from adverse events related to our product candidates, biotechnology or cell therapy, engineered cell therapy or encapsulated cell therapy fields, competitive clinical trials for similar patient populations or for other reasons, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of our product candidates may be delayed. These delays could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of the clinical trials altogether.

Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- size of the patient population and process for identifying patients;
- design of the trial protocol;
- availability and efficacy of approved medications for the disease under investigation;
- convenience and ease of administration compared to approved medications for the disease under investigation and the willingness of patients to undergo the surgical procedures necessary to administer our product candidates, such as laparoscopy;
- ability to obtain and maintain patient informed consent;
- risk that enrolled patients will drop out before completion of the trial;
- eligibility and exclusion criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial;

- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- factors we may not be able to control, such as current or potential pandemics that may limit patients, principal investigators or staff or clinical site availability.

Our ability to successfully initiate, enroll, and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- different standards for the conduct of clinical trials;
- different standard-of-care for patients with a particular disease;
- difficulty in locating qualified local consultants, physicians, and partners; and
- potential burden of complying with a variety of foreign laws, medical standards, and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit, or terminate such clinical trials, or expand to additional jurisdictions, which could impose additional challenges on our company and expose us to risks. If we are not successful in conducting our clinical trials as planned, it would have an adverse effect on our business, financial condition, results of operations, and prospects.

Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize any of our product candidates in the United States or any other jurisdiction, and any such approval may be for a more narrow indication than we seek.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials, and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or a REMS. These regulatory authorities may require labeling that includes precautions or contraindications with respect to conditions of use, or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of any product candidates we may develop, including claims that are necessary for certain patient populations such as pediatric patients. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and materially adversely affect our business, financial condition, results of operations, and prospects.

To date, we have not submitted a biologics license application, or BLA, or other marketing authorization application to the FDA or similar drug approval submissions to comparable foreign regulatory authorities for any product candidate. Marketing approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product candidate testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our product candidates in those countries. The foreign regulatory approval process involves all of the risks associated with FDA approval. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our product candidates will be unrealized.

Interim, topline or preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data becomes available 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 preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. 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 agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which may harm our business, financial condition, results of operations, and prospects.

Our product candidates may be considered combination products involving a proprietary delivery approach, which may result in additional regulatory and other risks.

Because our SLTx platform represents a novel approach to cell-based therapy development, we could be asked to perform additional preclinical or clinical studies, as well as develop additional manufacturing procedures and protocols, before we are able to obtain regulatory approvals for our product candidates. Our product candidates are comprised of both allogeneic human cells, which means the cells are obtained from a human donor other than the patient, and sphere components, and therefore we expect our product candidates to be regulated as biologic combination products, such as a biologic-device combination products for administration directly to the abdominal cavity or, as a novel cell-based therapies, which may subject our product candidates to additional regulatory requirements, such as CMC, preclinical or clinical

requirements. If FDA regulates our product candidates as biologic-device combination products, we anticipate each component would be subject to the FDA medical requirements for that type of component. If that is the case, our delivery system device would be subject to FDA device requirements regarding design, performance, and validation, and human factor testing, as well as manufacturing requirements, including the FDA's Quality System regulations applicable to medical devices. Additionally, products that are regulated as biologic-device combination products would require coordination within the FDA for review of the product candidate's device and biologic components. The determination whether a combination product requires a single marketing application or two separate marketing applications for each component is made by the FDA on a case-by-case basis. Although a single marketing application may be sufficient for the approval of a combination product, the FDA may determine that separate marketing applications are necessary. This determination could significantly increase the resources and time required to bring our combination product to market. Although the FDA has systems in place for the review and approval of combination products such as ours, we may experience delays in the development and commercialization of our product candidates due to regulatory timing constraints and uncertainties in the product development and approval process, as well as coordination between two different centers within FDA responsible for review of the different components of the combination product.

Even if we, or any collaborators we may have, obtain marketing approvals for any product candidates we develop, the terms of approvals and ongoing regulation of our product candidates could require the substantial expenditure of resources and may limit how we, or they, manufacture and market our product candidates, which could materially impair our ability to generate revenue.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, import, export, adverse event reporting, storage, recordkeeping, advertising, and promotional activities for such product candidate, will be subject to extensive and ongoing requirements imposed by the FDA, EMA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, facility registration and drug listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping, and with respect to any medical device components of our product candidates, compliance with applicable provisions of the FDA's Quality System regulation. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition, and prospects.

In addition, later discovery of previously unknown problems with our products, manufacturers, or manufacturing processes, or failure to comply with regulatory requirements, may yield various negative consequences, including:

- restrictions on such products, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a medicine;
- restrictions on the distribution or use of a medicine;
- requirements to conduct additional post-marketing clinical trials;
- receipt of warning or untitled letters;

- withdrawal of the products from the market, or suspension of marketing approvals;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of our approved product candidates;
- fines, restitution, or disgorgement of profits or revenue;
- restrictions on future procurements with governmental authorities;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our medicines;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates, if approved, and adversely affect our business, financial condition, results of operations, and prospects.

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

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new biologics or modifications to licensed biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the United States government has shut down several times and certain regulatory agencies, 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.

Risks Related to Our Industry and Future Commercialization

Even if a product candidate receives marketing approval, such product candidate may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors, and others in the medical community necessary for commercial success.

The commercial success of our product candidates will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community. Even if a product candidate receives marketing approval, the product may nonetheless fail to gain sufficient market acceptance by physicians, patients,

healthcare payors, and others in the medical community. The degree of market acceptance of any product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in clinical trials;
- the potential and perceived advantages compared to alternative treatments;
- the limitation to our targeted patient population and limitations or warnings contained in approved labeling by the FDA or other regulatory authorities;
- the ability to offer our product candidates for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments, including the logistical challenges of administering product candidates with a short shelf life and the willingness of patients to undergo the surgical procedures necessary to administer our product candidates, such as interventional radiology guided placement;
- the clinical indications for which the product candidate is approved by the FDA, the EMA, or other regulatory agencies;
- the willingness of the target patient population to try novel therapies and of physicians to prescribe these therapies;
- product labeling or product insert requirements of the FDA, the EMA, or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

In addition, even if product candidates are approved, such products may not achieve an adequate level of acceptance, we may not generate significant product revenues, and we may not become profitable.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have limited experience in the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved medicine for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, some of our current and future product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for

which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

Factors that may inhibit our efforts to commercialize a product for MPS-1 or any other product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel;
- the inability of sales personnel to obtain access to physicians to discuss our product candidates;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- restricted or closed distribution channels that make it difficult to distribute product candidates to segments of the patient population;
- the lack of complementary medicines to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenues or the profitability of these product revenues to us may be lower than if we were to market and sell any product we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our products we may develop.

We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.

The development and commercialization of new therapeutic biologics is highly competitive. Moreover, the engineered cell therapy field is characterized by rapidly changing technologies, significant competition, and a strong emphasis on intellectual property. We will face competition with respect to any product candidates that we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the same disease indications as our product candidates, including endocrine, lysosomal diseases and other acute and chronic disorders. We may face intense competition from large pharmaceutical companies with extensive resources and established relationships in these patient communities. The current standard of care for T1D is highly competitive and established, and includes Novo Nordisk's Levemir and Tresiba, and Sanofi's Toujeo and Lantus. There are also diabetes programs in development at ViaCyte, Inc. and Vertex Pharmaceuticals, Inc., which may compete with any therapy to treat diabetes we may develop. Additionally, several large pharmaceutical companies and biotechnology companies currently market and sell products for the treatment of lysosomal disorders. This includes products developed by Amicus Therapeutics, Inc., BioMarin Pharmaceutical Inc., or BioMarin,

and Ultragenyx Pharmaceutical Inc., or Ultragenyx, among others. Any product candidates that we or our collaborators successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future that are approved to treat the same diseases for which we may obtain approval for our product candidates.

Many of our current or potential competitors, either alone or with their collaboration partners, may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize product candidates that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than the product candidates we may develop or that would render any of our product candidates obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their product candidates 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.

Our commercial opportunity may also be reduced or limited if we or our partners are unable to manufacture large, cryopreserved lots of our products candidates in a fully automated encapsulation system efficiently. Additionally, technologies developed by our competitors may render our product candidates, or our future developments, uneconomical or obsolete, and we may not be successful in marketing a product for MPS-1 or any other product candidates against competitors.

In addition, we could face litigation with respect to the validity and/or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any of our product candidates. Further, intellectual property protection for human cell lines, including the engineered cell components of our product candidates are dynamic and rapidly evolving. The scope of intellectual property protection for the human cell line(s) used in our platform may be limited, and our commercial opportunity may be reduced or limited if our competitors are able to acquire or develop the same or similar cell lines.

Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices, or healthcare reform initiatives, which would harm our business.

The regulations that govern pricing, and reimbursement for new medicines vary widely from country to country. Outside the United States, some countries require approval of the sale price of a medicine before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay or might even prevent our commercial launch of the product candidate, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product candidate in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates we may develop.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which reimbursement for these product candidates and related treatments will be available from government authorities, government healthcare programs, private health plans, and other organizations. Government authorities and third-party payors, such as private health plans, decide which medications they will pay for and establish reimbursement levels. A primary trend in the United States healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are challenging the prices charged for medical products and requiring that drug companies provide them with predetermined discounts from list prices. Novel medical products, if covered at all, may be subject to enhanced utilization management controls designed to ensure that the products are used only when

medically necessary. Such utilization management controls may discourage the prescription or use of a medical product by increasing the administrative burden associated with its prescription or creating coverage uncertainties for prescribers and patients. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, that the level of reimbursement will be adequate. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved product candidates, and coverage may be more limited than the purposes for which the product candidate is approved by the FDA, the EMA or other regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any product candidate will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new product candidates, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the product candidate and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost therapies or medicines and may be incorporated into existing payments for other services. Net prices for product candidates may be reduced by mandatory discounts or rebates required for government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved product candidates we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize medicines, and our overall financial condition.

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

Under the Biologics Price Competition and Innovation Act of 2009, or BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that a 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. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

Any of our product candidates approved as a biological product under a BLA may not qualify for the 12-year period of exclusivity or this exclusivity could be shortened due to congressional action or otherwise, or the FDA may not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. 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.

Due to the novel nature of our technologies and the potential for our product candidates to offer therapeutic benefit in a single administration or limited number of administrations, we face uncertainty related to pricing and reimbursement for these product candidates.

If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any such product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to our product candidates (e.g., for administration of our product candidate to patients) is also important. Inadequate reimbursement for such services may lead to physician and payor resistance and adversely affect our ability to market or

sell our product candidates. In addition, we may need to develop new reimbursement models in order to realize adequate value.

Payors may not be able or willing to adopt such new models, and patients may be unable to afford that portion of the cost that such models may require them to bear. If we determine such new models are necessary but we are unsuccessful in developing them, or if such models are not adopted by payors, our business, financial condition, results of operations, and prospects could be adversely affected.

We expect that coverage and reimbursement by government and private payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of any such product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by government authorities, private health plans, and other third-party payors. Payors may not be willing to pay high prices for a single administration. Coverage and reimbursement by a third-party payor may depend upon several 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.

Obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical, and cost-effectiveness data. There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize any product candidates we may develop. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment.

Moreover, the downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new product candidates such as ours. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any of our product candidates will be harmed.

If the market opportunities for our MPS-1 program or any other product candidates are smaller than we believe they are, our potential revenues may be adversely affected, and our business may suffer.

We focus certain research and product development pipelines and our product candidates on treatments for rare diseases including endocrine, lysosomal diseases and other acute and chronic disorders. Our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. For example, the approximate incidence of MPS-1 is one in 100,000 live births. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our product candidates or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects. In addition, the number of patients with these diseases who have the potential to benefit from treatment may turn out to be lower than expected if we are unable to treat certain patient populations such as pediatric subpopulations.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any medicines that we may develop.

We face an inherent risk of product liability exposure related to our human clinical trial for SIG-001 or any other product candidates for which we may initiate human clinical trials in the future. We will face an even greater liability risk if we commercially sell any product candidates that we may develop. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant time and costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any product candidates that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage when we begin clinical trials and if we successfully commercialize any medicine. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and any contract manufacturers and suppliers we engage with are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste. 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. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. 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, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies (under which we currently have an aggregate of approximately $15.0 million in coverage) specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an

amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, we may incur substantial costs in order to comply with current or future environmental, health, and safety laws, regulations, and permitting requirements. These current or future laws, regulations, and permitting requirements may impair our research, development, or production efforts. Failure to comply with these laws, regulations, and permitting requirements also may result in substantial fines, penalties, or other sanctions or business disruption, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Any third-party contract manufacturers and suppliers we engage with will also be subject to these and other environmental, health, and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our technologies are novel, and any product candidates we develop may be complex and difficult to manufacture on a clinical or commercial scale. We could experience delays in satisfying regulatory authorities or production problems that result in delays in our development or commercialization programs, limit the supply of our product candidates we may develop, or otherwise harm our business.

Our SLTx platform is novel and the manufacture of products on the basis of our platform is untested at a large scale. Any current and future product candidates will likely require processing steps that are more complex than those required for most small molecule pharmaceuticals and traditional biologics. Moreover, unlike small molecules, the physical and chemical properties of various components in our product candidates generally cannot be fully characterized. As a result, assays of the finished drug product may not be sufficient to ensure that the product will perform in the intended manner. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims, insufficient inventory, or potentially delay progression of our regulatory filings. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs. If we or our contract manufacturers are unable to scale our manufacturing at the same levels of quality and efficiency, we may not be able to supply the required number of doses for clinical trials or commercial supply, and our business could be harmed.

As product candidates proceed through preclinical studies to clinical trials towards potential approval and commercialization, it is common that various aspects of the manufacturing methods and testing methods are changed along the way in an effort to optimize processes and results. Any such changes will require comparability studies to ensure that the manufacturing and testing method changes have not impacted on product quality and efficacy. Such changes may also require additional FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

In addition, the FDA, the EMA, the MHRA, and other regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA, the MHRA, or other regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Deviations in the manufacturing process, including those affecting quality attributes and stability of the product, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay clinical trials or product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations, and prospects.

We also may encounter problems hiring and retaining the experienced scientific, quality control, and manufacturing personnel needed to manage our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

The manufacture of biopharmaceutical products is complex and requires significant expertise, including the development of advanced manufacturing techniques and process controls. Manufacturers of cell therapy products often

encounter difficulties in production, particularly in scaling out and validating initial production and ensuring the absence of contamination. Given the nature of biologics manufacturing and the cell therapy products used in our early-stage programs there is a risk of contamination during manufacturing. For example, given the aseptic controls required for the manufacture of our product candidates, if contaminants are discovered in our supply of product candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. Any such contamination could materially harm our ability to produce product candidates on schedule and could delay our development programs and results of operations and cause reputational damage. We cannot assure you that any such issues relating to the manufacture of our product candidates will not occur in the future or that significant delays would not occur as a result of any such issue.

In addition, some of the raw materials that we anticipate will be required in our manufacturing process are derived from biologic sources, including Fetal Bovine Serum, which is used in our cell culture process, and our alginates, which are naturally occurring polymers derived from seaweed. Such raw materials can be difficult to procure and may be subject to contamination or recall. A material shortage, recall, or restriction on the use of biologically derived substances in the manufacture of any of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially harm our development timelines and our business, financial condition, results of operations, and prospects.

Any problems in our manufacturing process or the facilities with which we contract to make, store or ship our product candidates or any problems caused by us, our vendors or other factors not in our control could result in the loss of usable product or prevent or delay the delivery of product candidates to patients in our clinical trials. Any such loss or delay could materially delay our development timelines and harm our business, financial condition and results of operations. Such losses or delays could also make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs.

We purchase some of the starting material for our product candidates from a single source or a limited number of suppliers, and the partial or complete loss of one of these suppliers could cause production delays, clinical trial delays, substantial loss of revenue and contract liability to third parties.

We source a critical raw material used in our sphere alginate from a single supplier. A limited supply of this raw material and other raw materials with a limited number of suppliers could cause production delays, clinical trial delays, substantial lost revenue opportunities or contract liabilities to third parties. For example, there are only a limited number of qualified suppliers, and in some cases single source suppliers, for the raw materials included in our SLTx platform, including our current supply of alginates. Any interruption in supply, diminution in quality of raw materials supplied to us or failure to procure such raw materials on commercially feasible terms could harm our business by delaying the progress of our preclinical studies and future clinical trials and by impeding commercialization of potential approved products or increasing our costs.

Additionally, our sphere alginate is derived from a naturally occurring seaweed. The availability or characteristics of this material may be impacted by disease to this species of seaweed, ocean pollution and climate change as a result of global warming.

Risks Related to Our Relationships with Third Parties

We have entered and may in the future enter into collaborations with third parties for the research, development, and commercialization of SIG-002 or any other potential product candidates. If any such collaborations are not successful or our existing partners do not perform as expected, we may not be able to capitalize on the market potential of those product candidates.

We have engaged and may in the future seek third-party collaborators for the research, development, and commercialization of certain of the product candidates we may develop. For example, pursuant to our agreement with Eli Lilly and Company, or Lilly, for the development of SIG-002, Lilly will be responsible for submitting an IND and all clinical development and commercialization activities following such IND submission, and may take over some or all of

the research activities prior to such IND submission, at its cost. We will therefore depend on Lilly to design and conduct their clinical studies. If we enter into similar collaboration agreements for any of our other product candidates, we may also depend on partners to design and conduct clinical trials. As a result, we may have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of SIG-002 or other product candidates we may decide to partner with third-party collaborators. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of our current or any future collaboration that we enter into.

Our current and any future collaborations involving our research programs or our current or any future product candidates pose numerous risks to us, including the following:

- Collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations.

- Collaborators may not pursue development and commercialization of any current or future product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates 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 any current or future product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.

- Collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates.

- Collaborators may not properly obtain, maintain, enforce, or defend our intellectual property or proprietary rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation.

- Disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources.

- We may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control.

- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates we may develop.

- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished, or terminated.

If our collaborations do not result in the successful development and commercialization of product candidates, or if Lilly or any of our other collaborators terminates its agreement with us, we may not receive any future research funding or milestones or royalty payments under the collaboration. If we do not receive the funding we expect under these

agreements, our development of product candidates could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval, and commercialization described in this Annual Report on Form 10-K apply to the activities of our collaborators.

These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement 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 several factors. If we license rights to any of our future product candidates, as we have with Lilly for the development and commercialization of SIG-002, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

If conflicts arise between our partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. If any of our partners terminate or breach our agreements with them, or otherwise fail to complete their obligations in a timely manner, it may have a detrimental effect on our financial position by reducing or eliminating the potential for us to receive technology access and license fees, milestones and royalties, reimbursement of development costs, as well as possibly requiring us to devote additional efforts and incur costs associated with pursuing internal development of product candidates. Furthermore, if our partners do not prioritize and commit sufficient resources to programs associated with our product candidates or collaboration product candidates, we or our partners may be unable to commercialize these product candidates, which would limit our ability to generate revenue and become profitable.

If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our product development and research programs and the potential commercialization of any of our current and future product candidates will require substantial additional cash to fund expenses. For some of the product candidates we may develop, we may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. For example, we have partnered with Lilly for the development and commercialization of SIG-002 for the treatment of T1D.

We face significant competition in seeking appropriate collaborators. Whether we 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. Those factors may include preclinical results, the design or results of clinical trials, the likelihood of approval by the FDA, the EMA, the MHRA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us.

Collaboration agreements may also restrict us from entering into future agreements on certain terms with potential collaborators or from using intellectual property and product candidates resulting from such collaboration. Collaborations are complex 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.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce

or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to develop product candidates or bring them to market and generate product revenue.

We expect to rely on third parties to conduct our clinical trials and conduct some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing.

We expect to rely on third parties, such as CROs, medical institutions, and clinical investigators, to conduct our clinical trials. We currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical testing. Any of our collaborators and partners may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it may delay our product development activities.

Our reliance on third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, even if we rely on CROs to conduct our future clinical trials, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the study protocol for the trial. Moreover, the FDA, the EMA, the MHRA and other regulatory authorities will require us to comply with GCP requirements for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Although we intend to design the clinical trials for the majority of our product candidates, CROs will conduct some or all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical studies and clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff.

Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs and other third parties do not perform preclinical studies and future clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed or prevented, we may not be able to obtain regulatory

approval and commercialize our product candidates, or our development programs may be materially and irreversibly harmed.

We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our medicines, producing additional losses and depriving us of product revenue.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Additionally, CROs may lack the capacity to absorb higher workloads or take on additional capacity to support our needs. 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 have a material adverse impact on our business, financial condition and prospects.

Because we 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 lack the internal capability to manufacture any product candidates at clinical or commercial scale under cGMP conditions. The facilities used by our CMOs to manufacture our product candidates must be acceptable to the FDA and other comparable foreign regulatory agencies pursuant to inspections that would be conducted after we submit our marketing application or relevant foreign regulatory submission to the applicable regulatory agency. Our clinical development product supplies may be limited, interrupted or may not be of satisfactory quality or continue to be available at acceptable prices. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, they will not be able to secure or maintain regulatory approval for their manufacturing facilities. Any replacement of our CMOs could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for our product candidates is subject to FDA and foreign regulatory authority review. 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. We have no direct control over our CMOs' ability to maintain adequate quality control, quality assurance and qualified personnel. In the event that any of our manufacturers fails to comply with regulatory 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, and that the material manufactured in the new facility is comparable to the material manufactured in the original facility. 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. Our reliance on contract manufacturers also exposes us

to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information.

We expect to continue to rely on third-party CMOs if we receive regulatory approval for any product candidate. 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 our product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical studies of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for our product candidates;
- loss of the cooperation of an existing or future strategic partner;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- a requirement 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.

We, or our third-party manufacturers, may be unable to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any.

In order to conduct clinical studies of our product candidates and commercialize any approved product candidates, we, or our manufacturing partners, will need to manufacture them in large quantities. We, or our 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 studies 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 significantly harm our business. If we are unable to obtain or maintain third-party manufacturing for commercial supply of product candidates, or to do so on commercially reasonable terms, or if we are unable to develop our own manufacturing capabilities, we may not be able to develop and commercialize our product candidates successfully.

Risks Related to Our Intellectual Property

Our rights to develop and commercialize our SLTx platform technologies and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

A significant portion of our intellectual property portfolio has been licensed from third parties, and our licensors may not always act in our best interest. If we fail to comply with our obligations under our intellectual property licenses, if the licenses are terminated, or if disputes regarding these licenses arise, we could lose significant rights that are important to our business.

We have licensed and are dependent on certain patent rights and proprietary technology from third parties that are important or necessary to the development and commercialization of our technologies and product candidates. For example, we are a party to an exclusive patent license agreement with Massachusetts Institute of Technology, or MIT,

pursuant to which we in-license key patents and patent applications co-owned by MIT and Boston Children's Hospital, or BCH, covering our SLTx platform technologies and product candidates. We refer to this agreement as the MIT License. The MIT License imposes various diligence, milestone payment, royalty, insurance, and other obligations on us. If we fail to comply with these obligations, MIT may have the right to terminate our license, in which event we may not be able to develop or market our SLTx platform or any other technologies or product candidates covered by the licensed intellectual property. In addition, if we conclude that technology licensed to us under the MIT license or other agreements failed to prevent the PFO reported in a patient in our Phase 1/2 clinical trial of SIG-001, such licenses may also be less valuable to us. In the future, we may also enter into additional license agreements that are material to the development or commercialization of our product candidates, and that may impose similar obligations as in the MIT License. For example, if we are required to license additional technology in order to change the development of our SLTx platform, we may not be able to enter into such licenses with third parties on reasonable terms if at all.

These and other licenses may not provide sufficient rights to use such intellectual property, including cell lines or therapeutic protein sequences, in all relevant fields of use and in all territories in which we may wish to develop or commercialize our SLTx platform technologies and product candidates in the future. If we determine that rights to excluded fields or territories are necessary to commercialize our product candidates or maintain our competitive advantage, we may need to obtain additional licenses in order to continue developing, manufacturing or marketing our product candidates. We may not be able to obtain such licenses on an exclusive basis, on commercially reasonable terms, or at all, which could prevent us from commercializing our product candidates or allow our competitors or others the chance to access technology that is important to our business.

We do not have complete control in the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. For example, pursuant to the MIT License, MIT retains control of preparation, filing, prosecution, and maintenance. We cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, and maintained in a manner consistent with the best interests of our business. Also, in certain circumstances, MIT has the right to enforce and defend the licensed patents and patent applications. It is possible that any licensor enforcement of patents against infringers or defense of patents against challenges of validity or claims of enforceability may be less vigorous than if we had conducted them ourselves, or may not be conducted in accordance with our best interests. If we or our licensors fail to prosecute, maintain, enforce, and defend such patents, or if we or our licensors lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize our product candidates that are the subject of such licensed rights could be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products.

Our licensors may not be the sole and exclusive owners or may not have sole and exclusive control of the patents, patent applications and technology we in-licensed. If other third parties have rights to any of such in-licensed intellectual property, they may be able to license such intellectual property to our competitors, and our competitors could market competing products and technology. In addition, our rights to our in-licensed patents, patent applications and technology are dependent, in part, on inter-institutional or other operating agreements between the joint owners of such intellectual property. If one or more of such joint owners breaches such inter-institutional or operating agreements, our rights to such in-licensed intellectual property may be adversely affected. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Furthermore, inventions contained within some of our in-licensed intellectual property, including patents and patent applications licensed from MIT, were made using funding from the United States government, and, in some cases, private, non-profit organizations. We rely on our licensors to ensure compliance with applicable obligations arising from such funding, such as timely reporting of the filing of patent applications arising out of the funded research and licenses granted to such patent applications. The failure of our licensors to meet their obligations may lead to a loss of rights to the relevant licensed intellectual property or the unenforceability of relevant patents.

Also, university licensors, governments and other funding entities could have certain rights in our in-licensed patents and technology. For example, in the MIT License, MIT and BCH retain the right on behalf of themselves and all other non-profit research institutions to practice under the licensed patent rights for non-profit research, teaching and educational purposes, including sponsored research and collaborations, and the United States government retains a

non-exclusive license authorizing the United States government to use the inventions or to have others use the invention on its behalf. If the United States government decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. The United States government's rights may also permit it to disclose the funded inventions and technology to third parties and to exercise march-in rights to use or allow third parties to use the technology we have licensed that was developed using United States government funding. The United States government may also exercise its march-in rights if it determines that action is necessary because we or our licensors failed to achieve practical application of the United States government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to United States industry. In addition, our rights in such in-licensed United States government-funded inventions may be subject to certain requirements to manufacture product candidates embodying such inventions in the United States. Any of the foregoing could harm our business, financial condition, results of operations, and prospects significantly.

In the event any of our third-party licensors determine that, in spite of our efforts, we have materially breached a license agreement or have failed to meet certain obligations thereunder, it may elect to terminate the applicable license agreement or, in some cases, one or more license(s) under the applicable license agreement and such termination could result in us no longer having the ability to develop and commercialize product candidates and technology covered by that license agreement or license. In the event of such termination of a third-party in-license, or if the underlying patents under a third-party in-license fail to provide the intended exclusivity, competitors could have the freedom to seek regulatory approval of, and to market, products identical to ours. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties, or these agreements are terminated, or we otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We have entered into license agreements with third parties and may need to obtain additional licenses from our existing licensors and others to advance our research or allow commercialization of our product candidates. It is possible that we may be unable to obtain any additional licenses at a reasonable cost or on reasonable terms, if at all. In either event, we may be required to expend significant time and resources to redesign our technologies, product candidates, or the methods for manufacturing them or to develop or license replacement technologies, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

In the MIT License, we have the first right to bring any actions against any third party for infringing on the patents we have exclusively licensed. Certain of our license agreements, including the MIT License, also require us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. In spite of our efforts, our licensors might conclude that we have materially breached our obligations under such license agreements, including as a result of delays of our development milestones, and might therefore terminate the license agreements, thereby potentially removing or limiting our ability to develop and commercialize products and technologies covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties could have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of our SLTx platform technologies or product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and growth prospects. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technologies and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;

- the sublicensing of patent and other rights to third parties under our collaborative development relationships;

- our diligence obligations under the license agreement with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates and what activities satisfy those diligence obligations;

- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners;

- the effects of termination; and

- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. As a result, any termination of or disputes over our intellectual property licenses could result in the delay of our development and commercialization of our SLTx platform or other product candidates, the loss of our ability to develop and commercialize our SLTx platform or other product candidates, or our loss of other significant rights, any of which could have a material adverse effect on our business, financial conditions, results of operations, and prospects. It is also possible that a third party could be granted limited licenses to some of the same technology, in certain circumstances. For more information regarding our obligations in these agreements, please see "Business—License and Collaboration Agreements."

If we are unable to obtain and maintain patent and other intellectual property protection for our product candidates and for our SLTx platform, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technologies similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop, and our SLTx platform may be adversely affected.

Our commercial success will depend in large part on our ability to obtain and maintain patent, trademark, trade secret and other intellectual property protection of our SLTx platform technologies, product candidates and other technologies, methods used to manufacture them and methods of treatment, as well as successfully defending our patent and other intellectual property rights against third-party challenges. It is difficult, complex, time consuming and costly to protect cell-based technology, including our SLTx platform technologies. For example, important individual components of our platform and our product candidates may be in the prior art and available to third parties, and we may not be able to prevent use of such components in products that would compete with our product candidates. Our ability to stop unauthorized third parties from making, using, selling, offering to sell, importing or otherwise commercializing products similar to our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

We seek to protect our proprietary position by continuing to develop our own intellectual property and in-licensed intellectual property relating to our SLTx platform technologies and product candidates in the United States and abroad. If we or our licensors are unable to obtain or maintain patent protection with respect to our SLTx platform technologies and product candidates we may develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technologies similar or identical to ours and our ability to commercialize our product candidates may be adversely affected.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely

manner in the United States and other important markets. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends, in part, on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or any licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. The field of cell-based therapies has been the subject of extensive patenting activity. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain, and we may become involved in complex and costly litigation. Our pending and future patent applications may not result in patents being issued that protect our SLTx platform technologies or any of our current and future product candidates or that effectively prevent others from commercializing competitive technologies and product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and the scope of a patent claim may be reinterpreted after issuance. Even if our current or future owned and in-licensed patent applications issue as patents, the patents may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether any of our SLTx platform advances and any of our current and future product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

In addition, 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 intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Our owned patent applications and in-licensed patents and patent applications and other intellectual property may be subject to priority disputes or to inventorship disputes and similar proceedings.

We or our licensors may be subject to claims that former employees, collaborators, or other third parties have an interest in our owned patent applications or in-licensed patents, patent applications, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our current or any future product candidates. While it is our policy to require our employees and contractors who may be involved in the 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 develops intellectual property that we regard as our own. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership of our owned patent applications, in-licensed patents or patent applications, trade secrets or other intellectual property. If we or our licensors are unsuccessful in defending any such claims or disputes, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or the exclusive right to use, our owned or in-licensed patents or other intellectual property that is important to our current or any future product candidates. Even if we or our licensors are successful in defending against such claims, litigation could result in substantial costs and be a

distraction to management and other employees. Any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations, or prospects.

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

We have limited intellectual property rights outside the United States. The process for obtaining patent protection outside the United States is particularly difficult, expensive, time consuming, and complex. Thus, 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 be less extensive than those in the United States. In addition, the laws of foreign countries do not protect intellectual property rights to the same extent as federal and state laws of the United States. In addition, our intellectual property license agreements may not always include worldwide rights. Consequently, we may not be able to prevent third parties from practicing our owned and licensed inventions in all countries outside the United States, or from selling or importing products made using such inventions in and into the United States or other jurisdictions. Competitors may use our owned and licensed technologies in jurisdictions where we have not obtained patent protection, or in which our license rights are non-exclusive, 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 product candidates and our patents 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 biotechnology and pharmaceutical 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 intellectual property and proprietary rights generally. Proceedings to enforce our patents and 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. Moreover, 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. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

We may not be successful in acquiring or in-licensing necessary rights to key technologies or any product candidates we may develop.

We currently have rights to intellectual property, through licenses from third parties, to identify and develop product candidates, and we may seek to in-license additional rights to key components of our SLTx platform. We may also seek to in-license rights to develop improvements to our SLTx platform or expand our product candidate pipeline. The future growth of our business may depend in part on our ability to in-license or otherwise acquire the rights to additional product candidates and technologies. Although we have succeeded in licensing technologies from third-party licensees including MIT in the past, we cannot assure you that we will be able to in-license or acquire the rights to any product candidates or technologies from third parties on acceptable terms or at all.

We may enter into agreements with third-party licensors that provide that our field of use excludes particular fields. If we determine that rights to such fields are necessary to commercialize our product candidates or maintain our competitive advantage, we may need to obtain a license from such third parties in order to continue developing, manufacturing or marketing our product candidates. We may not be able to obtain such a license on an exclusive basis, on commercially reasonable terms, or at all, which could prevent us from commercializing our product candidates or allow our competitors or others the chance to access technology that is important to our business.

Furthermore, there has been extensive patenting activity in the fields of engineered cell therapy and encapsulated cell therapy, and pharmaceutical companies, biotechnology companies, and academic institutions are competing with us or are expected to compete with us in the field of cell therapy and filing patent applications potentially relevant to our business. Thus, there may be third-party patent applications, currently pending or filed in the future, that, if issued, may relate to our SLTx platform or product candidates. In order to market our product candidates, we may find it necessary or prudent to obtain licenses from such third-party intellectual property holders. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for any of our product candidates. We may also require licenses from third parties for certain technologies related to preexisting cell therapies to be incorporated in our SLTx platform.

Additionally, we may collaborate with academic institutions 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. Even if we hold such an option, we may be unable to negotiate a license from the institution 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.

In addition, the licensing or acquisition of third-party intellectual property rights is a highly competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

The biotechnology and pharmaceutical industries have experienced substantial litigation and other proceedings regarding intellectual property rights, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and may prevent, delay or otherwise interfere with our product discovery and development efforts.

Our commercial success depends upon our ability and the ability of our collaborators and licensors to develop, manufacture, market, and sell our product candidates and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights 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 subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our SLTx platform technologies and any product candidates we may develop, including interference proceedings, post-grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the EPO. Numerous United States and foreign issued patents and pending patent applications that are owned by third parties exist in the fields in which we are developing our product candidates and they may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit.

As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our SLTx platform technologies and 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 therapies, products or their methods of use or manufacture. As with many technology-based products, there may be third-party patent applications that, if issued, may be construed to cover components of our SLTx platform and product candidates. There may also be third-party patents of which we are currently unaware with claims to technologies, compositions, methods of manufacture or methods of use.

Because of the large number of patents issued and patent applications filed in our fields, third parties may allege they have patent rights encompassing our product candidates, technologies or methods. Third parties may assert that we are employing their proprietary technology without authorization and may file patent infringement claims or lawsuit against us, and if we are found to infringe such third-party patents, we may be required to pay damages, cease commercialization of the infringing technology, or obtain a license from such third parties, which may not be available on commercially reasonable terms or at all.

Our ability to commercialize our product candidates in the United States and abroad may be adversely affected if we cannot obtain a license on commercially reasonable terms to relevant third-party patents that cover our product candidates or SLTx platform technologies. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize our product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such United States patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such United States. patent claims, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such United States patent. If we are found to infringe a third party's intellectual property rights, and we are unsuccessful in demonstrating that such patents are invalid or unenforceable, we could be required to obtain a license from such third party to continue developing, manufacturing, and marketing our product candidates and our technologies. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our SLTx platform technology or product candidates or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business. We also could be forced, including by court order, to cease developing, manufacturing, and commercializing the infringing technology or product candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects.

Defense of third-party claims of infringement of misappropriation, or violation of intellectual property rights involves substantial litigation expense and would be a substantial diversion of management and employee time and resources from our business. Some third-parties 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 have a material adverse effect on our business, financial condition, results of operations and prospects. There could also 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. Any of the foregoing events could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may become involved in lawsuits to protect or enforce our future patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful and could result in a finding that such patents are unenforceable or invalid.

Competitors may infringe our future patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. In addition, our future patents or the patents of our licensing partners also are, and may in the future become, involved in inventorship, priority, validity or enforceability disputes. Countering or defending against such claims can be expensive and time consuming. In an infringement proceeding, a court may decide that a patent owned or in-licensed by us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our owned and in-licensed patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly.

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 may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These types of mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). These types of proceedings could result in revocation or amendment to our patents such that they no longer cover our product candidates. The outcome for any particular patent following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our licensors, 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 technology and/or product candidates. Defense of these types of claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

We may choose to challenge the patentability of claims in a third party's United States or foreign patent, regardless of whether the claims are a threat to our SLTx platform technologies or product candidates. In the United States, this may be done by requesting that the USPTO review the patent claims in re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings. There are equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). We may choose to challenge third-party patents in the EPO and other foreign patent offices. Even if successful, 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, SLTx platform technologies or other proprietary technologies.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. 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, 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government 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 government fees on patents and applications are due to be paid to the USPTO and foreign patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. For our in-licensed patents and patent applications, we generally rely on

our licensors, including MIT, to pay these fees due to United States and patent agencies outside of the United States. For our owned patent applications, we rely on our outside patent counsel in the United States and in foreign countries to monitor these deadlines and to pay these fees when so instructed.

The USPTO and foreign patent agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We depend on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property, and for our owned patent applications, we engage counsel and other professionals to help us comply with these requirements. While an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations, however, in which non-compliance can result in a partial or complete loss of patent rights in the relevant jurisdiction. Were a noncompliance event to occur, our competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Changes in patent law in the United States and jurisdictions outside of the United States could diminish the value of patents in general, thereby impairing our ability to protect our SLTx platform technologies and product candidates.

As is the case with other biotech and pharmaceutical 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.

Changes in either the patent laws or interpretation of the patent laws could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of our issued patents. For example, in March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, the United States transitioned from a "first to invent" to a "first-to-file" patent system. Under a "first-to-file" system, assuming that other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on an invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either file any patent application related to our technologies or product candidates or invent any of the inventions claimed in our or our licensor's patents or patent applications. The America Invents Act also includes a number of other significant changes to United States patent law, including provisions that affect the way patent applications will be prosecuted, allowing third-party submission of prior art and establishing a new post-grant review system, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third-party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third-party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third-party as a defendant in a district court action. The effects of these changes are currently unclear as the USPTO continues to promulgate 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, only 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 the specific patents discussed in this filing have not been determined and would need to be reviewed. Therefore, 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.

In addition, recent United States Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain 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 validity and enforceability of patents, once obtained. Depending on future actions by the United States Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable

ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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. The terms of individual patents depend upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest non-provisional filing date in the applicable country. However, the actual protection afforded by a patent varies from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Various extensions including patent term extension, or PTE, and patent term adjustment, or PTA, may be available, but the life of such extension, and the protection they afford, is limited. 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 and generics. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our product candidates might expire before or shortly after we or our partners commercialize those candidates. 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.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our technologies and product candidates, we also rely on trade secret protection, as well as confidentiality agreements, non-disclosure agreements and invention assignment agreements with our employees, consultants and third-parties, to protect our know-how and other confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable.

It is our policy to require our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed by 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 certain specified circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and that 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 exclusive property. In the case of consultants and other third-party service providers, the agreements provide us with certain rights to all inventions arising from the services. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technologies and processes. Additionally, 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. Any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable.

In addition to contractual measures, we try to protect the confidential nature of our proprietary information through other appropriate precautions, such as physical and technological security measures. However, trade secrets and know-how can be difficult to protect. These 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 any recourse we might take against this type of misconduct may not provide an adequate remedy to protect our interests fully. In addition, our trade secrets may be independently developed by others in a manner that could prevent us from receiving legal recourse. If any of our confidential or proprietary information, such as our trade

secrets, were to be disclosed or misappropriated, or if any of that information was independently developed by a competitor, our competitive position could be harmed.

In addition, some courts inside and outside the United States are sometimes less willing or unwilling to protect trade secrets. If we choose to go to court to stop a third-party from using any of our trade secrets, we may incur substantial costs. Even if we are successful, these types of lawsuits may consume our time and other resources. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Third parties may assert that our employees, consultants, or advisors have wrongfully used or disclosed confidential information or misappropriated trade secrets.

As is common in the biotechnology and pharmaceutical industries, we employ individuals that are currently or were previously employed at universities, research institutions or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and advisors 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 these individuals have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. We may then have to pursue litigation 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 could result in substantial costs and be a distraction to our technical and management personnel from their normal responsibilities. 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, that perception 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, and we may not have sufficient financial or other resources to adequately conduct this type of litigation or proceedings. For example, some of our competitors may be able to sustain the costs of this type of litigation or proceedings more effectively than we can because of their substantially greater financial resources. In any case, uncertainties resulting from the initiation and continuation of intellectual property litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

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 may be adversely affected.

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

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- any of our current and future product candidates, if approved, will eventually become commercially available in generic or biosimilar product forms;

- others may be able to make cell therapy products that are similar to any of our current and future product candidates or utilize similar cell therapy technology but that are not covered by the claims of the patents that we license or may own in the future;

- we, or our licensors or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;

- we, or our licensors or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;

- we, or our licensors or current or future collaborators, may fail to meet our obligations to the United States government regarding any in-licensed patents and patent applications funded by United States government grants, leading to the loss or unenforceability of patent rights;

- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;

- it is possible that our pending, owned or licensed patent applications or those that we may own or license in the future will not lead to issued patents;

- it is possible that there are prior public disclosures that could invalidate our owned or in-licensed patents, or parts of 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 product candidates or technology similar to ours;

- 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;

- issued patents that we hold rights to may be held invalid, unenforceable, or narrowed in scope, including as a result of legal challenges by our competitors;

- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;

- the laws of foreign countries may not protect our proprietary rights or the proprietary rights of our licensors or current or future collaborators to the same extent as the laws of the United States;

- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes that design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;

- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

- we have engaged in scientific collaborations in the past and will continue to do so in the future and our collaborators may develop adjacent or competing products that are outside the scope of our patents;

- we may not develop additional proprietary technologies that are patentable;

- any product candidates we develop may be covered by third parties' patents or other exclusive rights;

- the patents of others may harm our business; or

- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third-party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Regulatory and Compliance Matters

Our relationships with healthcare providers, physicians, and third-party payors will be subject to applicable anti-kickback, fraud and abuse, anti-bribery 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.

Our operations and arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, many of which will apply only if and when we market a product, include the following:

- federal false claims, false statements and civil monetary penalties laws prohibiting, among other things, any person from knowingly presenting, or causing to be presented, a false claim for payment of government funds or knowingly making, or causing to be made, a false statement to get a false claim paid;

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, or the purchasing or ordering of, a good or service for which payment may be made under federal healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which, in addition to privacy protections applicable to healthcare providers and other entities, prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to 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;

- the federal Food, Drug, and Cosmetic Act, or the FDCA, which among other things, strictly regulates pharmaceutical marketing, prohibits manufacturers from marketing such products for off-label use and regulates the distribution of samples;

- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs;

- the so-called "federal sunshine" law under the Affordable Care Act, which requires pharmaceutical companies to monitor and report certain financial interactions with certain healthcare providers as well as ownership and investment interests held by physicians and their immediate family members to the Centers for Medicare & Medicaid Services within the United States Department of Health and Human Services for re-disclosure to the public; and

- analogous state and foreign laws and regulations, such as state anti-kickback, anti-bribery and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws also require pharmaceutical companies to comply with specific compliance standards, restrict financial interactions between pharmaceutical companies and healthcare providers, require pharmaceutical companies to report information related to payments to health care providers or marketing expenditures, or require pharmaceutical companies to report certain pricing information.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Given the breadth of the laws and regulations, limited guidance for certain laws and regulations and evolving government interpretations of the laws and regulations, governmental authorities may possibly conclude that our business practices may not comply with healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

When carrying out any activity or inducement within the U.K. or EU designed to promote the prescription, supply, sale or consumption of medicinal products to persons qualified to prescribe or supply them (including, for example, physicians), no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. The provision of benefits or advantages to such individuals more generally is also governed by the national anti-bribery laws of the U.K. and the EU member states, such as the U.K. Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment, or in being excluded from public tenders for our products.

Payments made by biopharmaceutical companies to healthcare organizations, healthcare professionals (including physicians) and patient organizations in the U.K. and EU are required to be publicly disclosed. Direct and indirect payments and transfers of value are caught, including donations, grants, sponsorships, hospitality, fees for research and development, consultancy services and gifts. Moreover, in some EU Members States, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the relevant regulatory authorities. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the U.K. and EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Healthcare and other reform legislation may increase the difficulty and cost for us and any collaborators we may have to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been and continue to be ongoing efforts to implement legislative and regulatory changes regarding the healthcare system. Such changes could prevent or delay marketing approval of any product candidates that we may develop, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Although we cannot predict what healthcare or other reform efforts will be successful, such efforts may result in more rigorous coverage criteria, in additional downward pressure on the price that we, or our future collaborators, may receive for any approved products or in other consequences that may adversely affect our ability to achieve or maintain profitability.

In the United States, the federal government and individual states have aggressively pursued healthcare reform, as evidenced by the passing of the Affordable Care Act and the ongoing efforts to modify or repeal that legislation. The Affordable Care Act substantially changed the way healthcare is financed by both governmental and private insurers and contains a number of provisions that affect coverage and reimbursement of drug products and/or that could potentially reduce the demand for pharmaceutical products such as increasing drug rebates under state Medicaid programs for brand name prescription drugs and extending those rebates to Medicaid managed care and assessing a fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid. The Affordable Care Act has been subject to modification and additional modifications may occur. There are,

and may continue to be, judicial challenges. Other health care reform efforts beyond the Affordable Care Act, including efforts related to drug coverage and pricing, have been ongoing and a number of reforms have been enacted under the Biden Administration. We cannot predict the ultimate content, timing or effect of any federal and state reform efforts. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results, and we cannot predict how future federal or state legislative, judicial or administrative changes relating to healthcare reform will affect our business.

Federal and state governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, waivers from Medicaid drug rebate law requirements, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. The private sector has also sought to control healthcare costs by limiting coverage or reimbursement or requiring discounts and rebates on products. We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business. Any cost containment measures could significantly decrease the available coverage and the price we might establish for our products, which would have an adverse effect on our net revenues and operating results.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations for biological products will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval and decision-making processes may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We intend to seek orphan drug designation for our product candidates, but any orphan drug designations we receive may not confer marketing exclusivity or other expected benefits.

We may not be able to obtain orphan drug designation or similar designations in other jurisdictions for our product candidates, and previously granted orphan drug designations may be revoked. Any product candidates we may develop for prevalent diseases, such as diabetes, will not be eligible to receive orphan drug designation.

Even if we obtain United States orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different product candidates can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product candidate for the same condition if the FDA concludes that the later product candidate is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care compared with the product that has orphan exclusivity. The EU has its own criteria for designation as an orphan medicine but, as in the United States, orphan market exclusivity may not apply to the extent any further applicant can establish that its medicinal product is safer, more effective or otherwise clinically superior. Orphan drug exclusivity in the United States or the EU may also be lost if the FDA or EMA, respectively, determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

On August 3, 2017, the Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Our employees, principal investigators, consultants, and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, consultants, and commercial partners, and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU, the United Kingdom and other jurisdictions, provide accurate information to the FDA, the EMA, the United Kingdom and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA, the EMA, the MHRA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and 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 government investigations or other actions or lawsuits stemming from a failure to comply with these laws or 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, financial condition, results of operations, and prospects, including the imposition of significant fines or other sanctions.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates outside of the United States and require us to develop and implement costly compliance programs.

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act, or FCPA, prohibits any United States 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 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. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Similarly, the U.K. Bribery Act 2010 has extra-territorial effect for companies and individuals having a connection with the United Kingdom. The U.K. Bribery Act prohibits inducements both to public officials and private individuals and organizations. Compliance with the FCPA and the U.K. Bribery Act 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-United States nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our business outside of the United States, we will be required 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 development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting.

Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the United States government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on United States exchanges for violations of the FCPA's accounting provisions.

We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies and contractual obligations could adversely affect our business.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the United States and EU. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. We cannot be sure how these evolving laws and regulations will be interpreted, enforced or applied to our operations. Failure to comply with any of these laws and regulations could result in contractual liabilities as well as enforcement action against us. As a result, we could be subject to fines, claims for damages by affected individuals, negative publicity, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects. Applicable privacy laws and court decisions in the EU could also impact our ability to transfer personal data internationally.

Within the United States, there are numerous federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of personally identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected information has been handled in compliance with the various applicable requirements and our contractual obligations can be complex and may be subject to changing interpretation.

Additionally, the California Consumer Privacy Act, or the CCPA, became effective on January 1, 2020 with enforcement beginning July 1, 2020. The CCPA imposes stringent data privacy and data protection requirements for the data of California residents. Among other things, it requires covered companies to provide disclosures to California consumers and afford such consumers data protection rights, including the ability to opt-out of certain sales of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for certain data breaches that result in the loss of personal data that may increase the likelihood of, and risks associated with, data breach litigation. The effects of this legislation are potentially far-reaching and may require us to modify our data processing practices and policies and to incur substantial costs and expenses in an effort to comply.

Any data we may collect from patients enrolled in future clinical trials in the United Kingdom or the EU will be, subject to the General Data Protection Regulation, or GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill. Additionally, on July 16, 2020 the CJEU, Europe's highest court, held in the Schrems II case that the EU US Privacy Shield, a mechanism for the transfer of personal data from the EU to the United States, was invalid. The impact of this

decision on the ability to lawfully transfer personal information from the EU to the United States, has led to increased scrutiny on data transfers from the European Economic Area to the United States generally and may increase our costs of compliance with data privacy legislation.

Data privacy regulations and data privacy remain an evolving landscape at both the domestic and international level, with new regulations coming into effect, such as the California Consumer Privacy Act, and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape and such changes may require ongoing modifications to our policies, procedures and systems.

Risks Related to Employee and Operations Matters and Information Technology

Our future success depends on our ability to retain our Chief Executive Officer and other key executives and to attract, retain, and motivate qualified personnel.

We are highly dependent on Dr. Rogerio Vivaldi Coelho, our Chief Executive Officer, as well as the other principal members of our management and scientific teams. Dr. Vivaldi and such other principal members are employed "at will," meaning we or they may terminate the employment at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development, and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing, business development, general and administrative and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel and recently observed increases in employee attrition and turnover in our industry. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, challenges or the failure to succeed in preclinical or clinical trials or applications for marketing approval, may make it more challenging to recruit and retain qualified personnel. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, including our scientific co-founders, may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. The inability to recruit, or loss of services of certain executives, key employees, consultants, or advisors, may impede the progress of our research, development, and commercialization objectives and have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our internal computer systems, or those of our third-party vendors, collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.

Our internal computer systems and those of our current and any future third-party vendors, collaborators and other contractors or consultants are vulnerable to damage, interruption or data theft from computer viruses, computer hackers, malicious code, employee theft or misuse, ransomware, social engineering (including phishing attacks), denial-of-service attacks, sophisticated nation-state and nation-state-supported actors, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Cybersecurity incidents, which may not be immediately or ever detected, are increasing in frequency and evolving in nature.

System failure, accident and security breach, could cause interruptions in our operations, or result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other disruptions. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If we were to experience a significant cybersecurity breach of our information systems or data, the costs associated with the investigation, remediation and potential notification of the breach to counter-parties and data subjects could be material. In addition, our

remediation efforts may not be successful. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, we could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary information.

To the extent that any disruption or security breach were to result in a loss of, or damage to, our or our third-party vendors', collaborators' or other contractors' or consultants' data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability including litigation exposure, penalties and fines, we could become the subject of regulatory action or investigation, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed. Any of the above could have a material adverse effect on our business, financial condition, results of operations or prospects. While we maintain cyber-liability insurance (covering security and privacy matters), such insurance may not be adequate to cover any losses experienced as a result of a cybersecurity incident.

A pandemic, epidemic, or outbreak of an infectious disease, such the COVID-19 pandemic, may materially and adversely affect our business and our financial results and could cause a disruption to the development or supply of our product candidates.

COVID-19, including the continued spread of new variants of the virus and spikes in infection rates, could adversely impact any preclinical or clinical trial operations in the United States and Europe, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography, and our ability to conduct preclinical studies with reduced laboratory capacity. For example, similar to other biotechnology companies, we have, and may in the future, experience delays in initiating IND-enabling studies, protocol deviations, enrolling in any clinical trials or dosing of patients in any clinical trials as well as in activating any trial sites.

The COVID-19 pandemic has also impacted, and may continue to impact, our third-party suppliers and manufacturers, CMOs and CROs, including through the effects of facility closures, reductions in operating hours, staggered shifts and other social distancing efforts, labor shortages, decreased productivity and unavailability of materials or components.

Risks Related to Our Common Stock

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

Our share price has been and may continue to be volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive product candidates or technologies;
- the timing and results of preclinical studies for any product candidates that we may develop;
- failure or discontinuation of any of our product development and research programs;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- developments or changing views regarding the use of engineered cell therapy and encapsulated cell therapy;
- commencement or termination of collaborations for our product development and research programs;
- regulatory or legal developments in the United States and other countries;

- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions, including due to the impacts of inflation; and
- the other factors described in this "Risk Factors" section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. The uncertain nature, magnitude and duration of hostilities stemming from the conflict in Ukraine, including the potential effects of sanctions limitations, retaliatory cyber-attacks on the world economy and markets, have contributed to increased market volatility and uncertainty. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. These fluctuations may be even more pronounced in the trading market for our stock. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

Insiders have substantial influence over us, which could limit your ability to affect the outcome of key transactions, including a change of control.

As of December 31, 2022, our directors and executive officers and their affiliates beneficially owned shares representing approximately 35.5% of our outstanding common stock. As a result, these stockholders, if they act together, are able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time consuming effort that needs to be reevaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding

the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business.

Our independent registered public accounting firm will not be required to formally attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 until we are no longer an emerging growth company or a smaller reporting company. At such time, our independent registered public accounting firm may issue a report that is adverse in the event it is not satisfied with the level at which our controls are documented, designed or operated. However, Section 404 of the Sarbanes-Oxley Act of 2002 requires management to furnish a report on our internal control over financial reporting. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing whether such controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting.

If either we are unable to conclude that we have effective internal control over financial reporting or, at the appropriate time, our independent auditors are unwilling or unable to provide us with an unqualified report on the effectiveness of our internal control over financial reporting as required by Section 404, investors may lose confidence in our operating results, the price of our common stock could decline and we may be subject to litigation or regulatory enforcement actions.

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years following our initial public offering. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes Oxley Act, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders is different than the information that is available with respect to other public companies. 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.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to not to "opt out" of the extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we may adopt the new or revised standard at the time private companies adopt the new or revised standard.

Further, even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. In addition, if we are a smaller reporting company, we would not be required to comply with the auditor

attestation requirements of Section 404 of the Sarbanes-Oxley Act. These exemptions and reduced disclosures in our SEC filings due to our status as a smaller reporting company may make it harder for investors to analyze our results of operations and financial prospects. We cannot predict if investors will 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 prices may be more volatile.

We do not expect to pay any dividends for the foreseeable future.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, any future credit facility may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

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

We have incurred substantial losses during our history, and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset a portion of future taxable income, if any, subject to expiration of such carryforwards in the case of carryforwards generated prior to 2018. Additionally, we continue to generate business tax credits, including research and development tax credits, which generally may be carried forward to offset a portion of future taxable income, if any, subject to expiration of such credit carryforwards. Under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. Our prior equity offerings and other changes in our stock ownership have resulted in such ownership changes. We may experience additional ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOLs or other pre-change tax attributes to offset United States federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. Additionally, for taxable years beginning after December 31, 2017, the deductibility of such United States federal net operating losses is limited to 80% of our taxable income in any future taxable year. There is a risk that due to legislative changes, regulatory changes, or other unforeseen reasons, our existing NOLs or business tax credits could expire or otherwise be unavailable to offset future income tax liabilities. At the state level, there may also be periods during which the use of NOLs or business tax credits is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For these reasons, we may not be able to realize a tax benefit from the use of our NOLs or tax credits, even if we attain profitability.

Provisions in our amended and restated certificate of incorporation, our amended and restated by-laws and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation, amended and restated by-laws and Delaware law contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. Our amended and restated certificate of incorporation and by-laws include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors;

- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- 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;
- provide that our directors may be removed for cause only;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorized our board of directors to modify, alter or repeal our amended and restated by-laws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock.

In addition, because we are incorporated in the State of Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, or the DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

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

Our amended and restated certificate of incorporation designates the state or federal courts within the State of Delaware as the exclusive forum for certain types of actions and proceedings that may be initiated by 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, subject to limited exceptions, the state or federal courts within the State of Delaware are exclusive forums for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated by-laws, (4) any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws or (5) any other action asserting a claim against us that is governed by the internal affairs doctrine; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or to any claim for which the federal courts have exclusive jurisdiction. Our amended and restated certificate of incorporation also provides that, unless we consent in writing to the selection of an alternative forum, the United States federal district courts shall be the exclusive forum for the resolution of any claims arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. This choice of 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 such lawsuits against us and our directors, officers and employees.

Alternatively, if a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

Item 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

Item 2. PROPERTIES

Our corporate office is located in Cambridge, Massachusetts where we lease a total of approximately 44,118 square feet of office and laboratory space that we use for our administrative, research and development and other activities. The term of the lease is scheduled to expire in February 2025. We are entitled to one option to extend the lease term on 22,746 square feet of office and laboratory space for an additional three years. We believe that our facilities are enough to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. LEGAL PROCEEDINGS

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm 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 Information

On December 4, 2020, our common stock began trading on the Nasdaq Global Select Market under the symbol "SGTX". Prior to that time, there was no public market for our common stock. Shares sold in our initial public offering on December 8, 2020 were priced at $18.00 per share.

On March 10, 2023, the last reported sales price of our common stock on the Nasdaq Global Select Market was $0.964 and as of March 10, 2023, there were approximately 26 holders of record of our common stock.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors our board of directors deems relevant, and subject to the restrictions contained in any future financing instruments. Our ability to pay cash dividends on our capital stock in the future may also be limited by the terms of any preferred securities we may issue or agreements governing any indebtedness we may incur.

Equity Compensation Plans

The information required with respect to this item is incorporated herein by reference to our Definitive Proxy Statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC no later than 120 days after the close of our year ended December 31, 2022.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. Reserved

Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the financial statements and notes included in Item 8 of this Annual Report on Form 10-K. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates and beliefs. Our actual results could differ materially from those discussed in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report, including, but not limited to, those set forth in "Cautionary Note Regarding Forward-Looking Statements" and "Risk Factors."

Overview

We are a preclinical stage biotechnology company pioneering a new class of therapeutics and seeking to develop functional cures for patients with acute and chronic diseases by providing stable and durable levels of therapeutic molecules to patients. We have developed our Shielded Living Therapeutics, or SLTx, platform, which combines advanced cell engineering with cutting-edge innovations in cell differentiation and biocompatible materials, and enables our product candidates to provide a wide range of functions or therapeutic molecules that may be missing or dysfunctional in patients. We are designing our product candidates to be off-the-shelf, durable, controllable and redosable, without requiring modification of the patient's genes or chronic suppression of the patient's immune system.

Since our inception, we have devoted substantially all of our efforts to raising capital, obtaining financing, filing and prosecuting patent applications, organizing and staffing our company and incurring research and development costs related to advancing our biomedical platform. We do not have any products approved for sale and have not generated any revenue from product sales. To date, we have funded our operations primarily with proceeds from sales of common stock and convertible preferred stock, payments received under our collaboration agreement with Lilly and proceeds from borrowings under our credit facilities. Through December 31, 2022, we have received gross proceeds of $144.9 million from the sale of common stock in the IPO, $142.4 million from sales of our convertible preferred stock and net proceeds of $19.8 million through borrowings under our loan and security agreement with Oxford Finance LLC, or the 2020 Credit Facility, partially offset by the $15.0 million repayment of debt from our 2019 Credit Facility. We have also partnered one of our encapsulation technology programs with Lilly. Under the terms of the partnership, we received an upfront payment of $62.5 million and we are eligible to receive additional milestone payments of up to $165.0 million upon achievement of certain regulatory milestones and sales-based milestones of up to $250.0 million for SIG-002. We are also eligible to receive tiered royalty payments in the mid-single digit to low-double digit percentages based on certain sales thresholds. Finally, Lilly is obligated to reimburse us for costs incurred to perform the research and development activities for the first developed product candidate, including costs up to $47.5 million. As of December 31, 2022 and 2021, we had $2.2 million and $0.1 million in accounts receivable and $1.3 million and $0 in unbilled accounts receivable with Lilly, respectively.

We have incurred significant operating losses since our inception. Our ability to generate any product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more of our product candidates. We reported net losses of $43.6 million and $77.3 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $256.8 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our current research programs and our preclinical development of product candidates from our current research programs;
- seek to identify additional research programs and additional product candidates;
- conduct additional preclinical studies for our product candidates;
- initiate clinical trials for our Mucopolysaccharidosis Type I, or MPS-1, program, or any other product candidates;

- comply with regulatory requirements established by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, and other comparable foreign regulatory authorities;
- seek marketing approvals for any of our product candidates;
- ultimately establish a sales, marketing, and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval;
- further develop our SLTx platform;
- hire additional research, development, manufacturing, quality, supply chain and commercial personnel;
- continue to hire and retain research and clinical personnel;
- add operational, financial, corporate development and management information systems and legal personnel, including personnel to support our product development and planned future commercialization efforts;
- expand our facilities;
- acquire or in-license product candidates, intellectual property and technologies;
- scale up manufacturing and supply chain capacity to meet future clinical and commercial demand, including scaling up processes for cell culture and automated encapsulation, and building or expanding our manufacturing capabilities or capacity, including future manufacturing facilities;
- file, prosecute, defend, and enforce our patent claims and other intellectual property rights, including patent infringement actions brought by third parties against us regarding our investigational medicines or actions by us challenging the patent or intellectual property rights of others, and provide reimbursement of third-party expenses related to our patent portfolio; and
- operate as a public company.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for one or more of our product candidates. If we obtain regulatory approval for any of our product candidates, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing and distribution. Further, we expect to continue to incur additional costs associated with operating as a public company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, or other capital sources, including collaborations with other companies and other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

Components of Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. Substantially all of our revenue to date has been derived from the collaboration agreement with Lilly, which we entered into in 2018.

If our development efforts for our product candidates are successful and result in regulatory approval or if we enter into license or collaboration agreements with third parties, we may generate revenue in the future from product sales, payments from license or collaboration agreements that we may enter into with third parties, or any combination thereof. We expect that our revenue for the next several years will be derived primarily from our collaboration agreement with Lilly as well as any additional collaborations that we may enter into in the future. We cannot provide assurance as to the timing of future milestone or royalty payments or that we will receive any of these payments at all.

Collaboration Revenue

In April 2018, we entered into a License and Collaboration Agreement with Lilly, or the 2018 Lilly Agreement. Under the 2018 Lilly Agreement, we granted Lilly an exclusive worldwide, royalty-bearing license, including the right to grant sublicenses, to our encapsulation technology applied to islet cells. We are responsible for our own costs and expenses associated with pre-clinical development of a product candidate, and completion of the studies and other criteria required for filing the first IND, up to $47.5 million. Lilly is responsible for filing the first IND, all subsequent clinical development and commercialization, all research, development and commercialization for any subsequent product candidates, as well as reimbursing us for research and development costs required for filing the first IND related to the first developed product candidate that exceed $47.5 million.

We evaluated the 2018 Lilly Agreement under ASC 606 and concluded at the outset that there were two performance obligations under the arrangement: (1) exclusive license to research, develop, manufacture and commercialize licensed products, initial technology transfer, research activities (including pre-IND supply), cell line development and supply and product trademark election, or the Combined Performance Obligation; and (2) requirement to supply Lilly with the licensed product related to Phase 1 clinical trial, or Phase 1 Supply. We determined that the $62.5 million upfront payment represents the entirety of the consideration to be included in the transaction price as of the outset of the arrangement. We allocated $56.6 million of the transaction price to the Combined Performance Obligation and $5.9 million of the transaction price to the Phase 1 Supply at the outset of the arrangement. We recognize revenue for the Combined Performance Obligation as the research and development services are provided using an input method, based on the cumulative costs incurred compared to the total estimated costs expected to be incurred to satisfy the Combined Performance Obligation. The transfer of control to the customer occurs over the time period that the research and development services are to be provided by us, and this cost-to-cost method is, in management's judgment, the best measure of progress toward satisfying this performance obligation. We have determined that the Phase 1 Supply will be satisfied at a point in time when the customer obtains control of each unit of product. Therefore, we will recognize revenue as shipments of the Phase 1 Supply are made to Lilly.

We reevaluate the transaction price and our total estimated costs expected to be incurred at the end of each reporting period and as uncertain events, such as changes to the expected timing and cost of certain research, development and manufacturing activities that we are responsible for, are resolved or other changes in circumstances occur, and, if necessary, we will adjust our estimate of the transaction price or our total estimated costs expected to be incurred.

Additional information regarding the 2018 Lilly Agreement can be found in Note 9 to our financial statements in this Annual Report on Form 10-K.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts and the development of our platform and product candidates. We expense research and development costs as incurred, which include:

- employee-related expenses, including salaries, bonuses, benefits, stock-based compensation, other related costs for those employees involved in research and development efforts;
- expenses incurred in connection with the preclinical development of our product candidates and research programs, including under agreements with third parties, such as consultants, contractors, and CROs;
- the cost of raw materials and developing and scaling our manufacturing process and manufacturing product candidates for use in our research and preclinical studies, including under agreements with third parties, such as consultants, contractors, and CMOs;
- laboratory supplies and research materials;
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and insurance; and
- payments made under third-party licensing agreements.

We expense research and development costs as incurred. Non-refundable advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed, or when it is no longer expected that the goods will be delivered or the services rendered. Upfront payments under license agreements are expensed upon receipt of the license, and annual maintenance fees under license agreements are expensed in the period in which they are incurred. Milestone payments under license agreements are accrued, with a corresponding expense being recognized, in the period in which the milestone is determined to be probable of achievement and the related amount is reasonably estimable.

Our direct external research and development expenses are tracked on a program-by-program basis, including our early-stage programs, and consist of costs that include fees, reimbursed materials, and other costs paid to consultants, contractors, contract manufacturing organizations or CMOs, and contract research organizations or CROs, in connection with our preclinical and manufacturing activities. Except for personnel expenses related to SIG-002, we do not allocate employee costs, costs associated with our discovery efforts, laboratory supplies and facilities expenses, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple programs and our platform and, as such, are not separately classified. The personnel expenses allocated to SIG-002 do not include stock-based compensation expense.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later stage clinical trials. We expect that our research and development expenses will increase substantially in connection with our planned preclinical and clinical development activities in the near term and in the future. At this time, we cannot accurately estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any of our product candidates. The successful development and commercialization of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the following:

- the timing and progress of preclinical and clinical development activities;

- the number and scope of preclinical and clinical programs we decide to pursue;
- raising additional funds necessary to complete preclinical and clinical development of and commercialize our product candidates;
- the progress of the development efforts of parties with whom we may enter into collaboration arrangements;
- our ability to maintain our current research and development programs and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the successful initiation and completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA, or any comparable foreign regulatory authority;
- the receipt and related terms of regulatory approvals from applicable regulatory authorities;
- the availability of raw materials for use in the production of our product candidates;
- our ability to consistently manufacture our product candidates for use in clinical trials;
- our ability to establish and operate a manufacturing facility, or secure manufacturing supply through relationships with third parties;
- our ability to obtain and maintain patents, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- our ability to protect our rights in our intellectual property portfolio;
- the commercialization of our product candidates, if and when approved;
- obtaining and maintaining third-party insurance coverage and adequate reimbursement;
- the acceptance of our product candidates, if approved, by patients, the medical community and third-party payors;
- competition with other products; and
- a continued acceptable safety profile of our therapies following approval.

A change in the outcome of any of these variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of these product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and personnel expenses, including stock-based compensation, for our personnel in executive, legal, finance and accounting, human resources, and other administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters; professional fees paid for accounting, auditing, consulting, and tax services; insurance costs; travel expenses; and facility costs not otherwise included in research and development expenses.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates. We also anticipate that we will incur significantly increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with operating as a public company. Additionally, if and when we believe a regulatory approval of a product candidate appears likely, we anticipate an increase in payroll and other employee-related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of that product candidate.

Other Income (Expense)

Interest Income

Interest income consists of interest earned on our cash, cash equivalents and marketable securities balances. We expect our interest income will fluctuate based on the timing and ability to raise additional funds as well as the amount of expenditures for our platform development and ongoing business operations.

Interest Expense

Interest expense consists of interest expense on outstanding borrowings under our loan and security agreements as well as amortization of debt discount and deferred financing costs.

Other Income, net

Other income consists primarily of insurance proceeds, sublease income, gain on the disposal of fixed assets and net foreign exchange losses.

Income Taxes

Since our inception, we have not recorded any income tax benefits for the net operating losses we have incurred in each year or for our earned research and development tax credits generated in each period, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating loss, or NOL, carryforwards and tax credit carryforwards will not be realized. We have recorded a full valuation allowance against our net deferred tax assets at each balance sheet date.

Critical Accounting Policies and Significant Judgments and Estimates

Our financial statements are prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of our financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events, and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our financial statements included elsewhere in this Annual Report on Form 10-K. We believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

To date, our revenues have consisted primarily of payments received related to the 2018 Lilly Agreement. We follow the provisions of ASC Topic 606, *Revenue from Contracts with Customers*, or ASC 606, for all contracts with

customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments.

Under ASC 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration that we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when, or as, we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract, determine those that are performance obligations and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, we perform the following five steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the assessment of the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when, or as we satisfy each performance obligation. As part of the accounting for arrangements under ASC 606, we must use significant judgment to determine: a) the performance obligations based on the determination under step (ii) above; b) the transaction price under step (iii) above; and c) the standalone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. We also use judgment to determine whether milestones or other variable consideration, except for royalties and sales-based milestones, should be included in the transaction price as described below. The transaction price is allocated to each performance obligation based on the relative stand-alone selling price of each performance obligation in the contract, and we recognize revenue based on those amounts when, or as, the performance obligations under the contract are satisfied.

The standalone selling price is the price at which an entity would sell a promised good or service separately to a customer. Management estimates the standalone selling price of each of the identified performance obligations in our customer contracts, maximizing the use of observable inputs. Because we have not sold the same goods or services in our contracts separately to any customers on a standalone basis and there are no similar observable transactions in the marketplace, we estimate the standalone selling price of each performance obligation in our customer arrangements based on our estimate of costs to be incurred to fulfil our obligations associated with the performance, plus a reasonable margin.

In assessing whether a license is distinct from the other promises, we consider relevant facts and circumstances of each arrangement, including the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, we consider whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining promises, whether the value of the license is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises, and whether it is separately identifiable from the remaining promises. We determined there were two distinct performance obligations at the outset of the 2018 Lilly Agreement, the Combined Performance Obligation and the Phase 1 Supply performance obligation.

For performance obligations which consist of licenses combined with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. The measure of progress, and the resulting periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the arrangement, which are subject to review by a joint research committee, or JRC. Such a change could have a material impact on the amount of revenue we record in future periods. We concluded that the transfer of control to the customer for the Combined Performance Obligation occurs over the time period that the research and development services are provided by us. We recognize revenue for the Combined

Performance Obligation as those services are provided using an input method, based on the cumulative costs incurred compared to the total estimated costs expected to be incurred to satisfy the Combined Performance Obligation. The cost-to-cost method is, in management's judgement, the best measure of progress towards satisfying the performance condition.

For the Phase 1 Supply performance obligation, which was determined to be a material right, the standalone selling price was estimated using the expected cost-plus margin approach. We determined that the Phase 1 Supply will be satisfied at a point in time when the customer obtains control of each unit of product. Therefore, we will recognize revenue as shipments of the Phase 1 Supply are made to Lilly.

At the inception of each arrangement that includes research, development or regulatory milestone payments, we evaluate whether the milestones are considered likely to be met and estimate the amount to be considered for inclusion in the transaction price using the most-likely-amount method. If it is probable that a significant reversal in the amount of cumulative revenue recognized would not occur, the associated milestone value is included in the transaction price. For milestone payments due upon events that are not within the control of us or the licensee, such as regulatory approvals, we are not able to assert that it is likely that the regulatory approval will be granted and that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur until those approvals are received. In making this assessment, we evaluate factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone. There is considerable judgment involved in determining whether it is probable that a significant reversal in the amount of cumulative revenue recognized would not occur. At the end of each subsequent reporting period we reevaluate the probability of achievement of all milestones subject to constraint and, if necessary, adjust our estimate of the overall transaction price of the arrangement. Any such adjustments are recorded on a cumulative catch-up basis, which would affect the amount of revenue and earnings in the period of adjustment. As of December 31, 2022, no milestones under the 2018 Lilly Agreement were included in the transaction price as no milestones had been deemed likely to be achieved or had been achieved.

We reevaluate the transaction price and our total estimated costs expected to be incurred at the end of each reporting period and as uncertain events, such as changes to the expected timing and cost of certain research, development and manufacturing activities that we are responsible for, are resolved or other changes in circumstances occur. If necessary, we will adjust our estimate of the transaction price or our total estimated costs expected to be incurred.

During the year ended December 31, 2022, consistent with the Company's presentation to the JRC, the Company revised its estimate of total costs to complete the activities under the 2018 Lilly Agreement to reflect the Company's experiences to date and the impact this has on its expected future research and development activities to satisfy the Combined Performance Obligation. During the year ended December 31, 2022, there has been an increase to the total estimated costs expected to be incurred of $13.5 million compared to the estimate as of December 31, 2021. The increase in total estimated costs impacted both the Company's estimated transaction price for the 2018 Lilly Agreement, as Lilly is obligated to reimburse the Company if the costs exceed $47.5 million to complete the services, and the Company's input method used to recognize revenue, as this measure compares the Company's cumulative costs incurred to the Company's total estimated costs expected to be incurred. During the year ended December 31, 2022, based on the allocation of total transaction price to each performance obligation using the relative stand-alone selling price of each performance obligation under the 2018 Lilly Agreement, the transaction price for the Combined Performance Obligation increased by $12.7 million and the Phase 1 supply performance obligation increased by $1.3 million.

We determined that our only contract liability under ASC 606 is deferred revenue. Amounts received prior to revenue recognition are recorded as deferred revenue in the balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion in the balance sheets. Amounts are recorded as accounts receivable and unbilled accounts receivable when our right to consideration is unconditional.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses. This process involves estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in the financial statements based on facts and circumstances known to us at that time. At each period end, we corroborate the accuracy of these estimates with the service providers and make adjustments, if necessary. Examples of estimated accrued research and development expenses include those related to fees paid to:

- Vendors in connection with discovery and preclinical development activities;
- CROs in connection with preclinical studies and testing; and
- CMOs in connection with the process development and scale up activities and the production of materials.

We record the expense and accrual related to contract research and manufacturing based on our estimates of the services received and efforts expended considering a number of factors, including our knowledge of the progress towards completion of the research, development, and manufacturing activities; invoicing to date under contracts; communication from the CROs, CMOs and other companies of any actual costs incurred during the period that have not yet been invoiced; and the costs included in the contracts and purchase orders. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We measure all stock-based awards granted to employees and directors based on their fair value on the date of the grant using the Black-Scholes option-pricing model for options or the market price of our common stock on the grant date for restricted stock units. Compensation expense for those awards is recognized over the requisite service period, which is generally the vesting period of the respective award for the employees and directors.

We use the straight-line method to record the expense of awards with only service-based vesting conditions. We record the expense of awards with performance-based vesting when we conclude that it is probable the performance condition will be achieved. The Black-Scholes option-pricing model uses as inputs the fair value of our common stock and assumptions we make for the volatility of our common stock, the expected term of our common stock options, the risk-free interest rate for a period that approximates the expected term of our common stock options, and our expected dividend yield.

Compensation expense for purchases under the Employee Stock Purchase Plan is recognized based on the fair value of the common stock estimated based on the closing price of our common stock as reported on the date of offering, less the purchase discount percentage provided for in the plan.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		Increase (Decrease)
	2022	2021	
	(in thousands)		
Revenue			
Collaboration revenue	$ 12,944	$ 9,599	$ 3,345
Operating expenses:			
Research and development	37,631	65,069	(27,438)
General and administrative	18,979	20,166	(1,187)
Total operating expenses	56,610	85,235	(28,625)
Loss from operations	(43,666)	(75,636)	31,970
Other income (expense):			
Interest income	946	258	688
Interest expense	(2,290)	(1,988)	(302)
Other income, net	1,449	55	1,394
Total other income (expense), net	105	(1,675)	1,780
Net loss	$ (43,561)	$ (77,311)	$ 33,750

Revenue

Revenue was $12.9 million for the year ended December 31, 2022, compared to $9.6 million for the year ended December 31, 2021. The Company recognizes revenue under the 2018 Lilly Agreement based on the input method, and as the costs incurred increased by $2.0 million during the year ended December 31, 2022, income recognized also increased. In addition, as the projected costs to complete certain activities decreased, there was an increase in recognized revenue.

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		Increase (Decrease)
	2022	2021	
	(in thousands)		
Direct research and development expenses by program:			
Diabetes program	$ 10,638	$ 8,532	$ 2,106
MPS-1 program	4,591	6,324	(1,733)
Platform and other early stage programs	10,094	29,853	(19,759)
Unallocated expenses			
Personnel expenses (including stock-based compensation)	9,483	15,822	(6,339)
Facility related and other	2,825	4,538	(1,713)
Total research and development expenses	$ 37,631	$ 65,069	$ (27,438)

Research and development expenses were $37.6 million for the year ended December 31, 2022, compared to $65.1 million for the year ended December 31, 2021. The decrease in research and development expenses was primarily related to decreased ongoing platform and other early-stage programs, MPS-1 program, facility related and other and personnel expenses, which were offset by increases in direct research and development expenses for our diabetes program.

The decrease in platform and pipeline development, MPS-1 program, personnel expenses, and the increase in the diabetes program expenses is primarily due to our reprioritization of the development of MPS-1, diabetes and platform optimization following the Company's restructuring activities in December 2021. The decrease in facility related and other expenses is primarily due to the sublease of a portion of our facility.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2022 were $19.0 million, compared to $20.2 million for the year ended December 31, 2021. General and administrative expenses decreased by $1.2 million as a result of decreased personnel expenses primarily in connection with our restructuring activities that occurred in December 2021.

Other Income (Expense), net

Other income (expense), net, primarily consists of insurance income, interest income, and interest expense. Other income (expense), net, for the year ended December 31, 2022 and 2021 was $0.1 million and ($1.7) million, respectively. The increase was primarily due to increased interest income associated with increased investment in marketable securities, insurance income and the gain on the sale of fixed assets, which was offset by increased interest expense due to higher interest rates on our credit agreement.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have incurred significant operating losses. We have not yet commercialized any of our product candidates and we do not expect to generate revenue from sales of any product candidates for the foreseeable future, if at all. To date, we have funded our operations primarily with proceeds from sales of common stock and convertible preferred stock, payments received under our collaboration agreement with Lilly and proceeds from borrowings under our credit facilities. Through December 31, 2022, we had received net proceeds of $131.8 million from the sale of common stock in the IPO, $141.9 million from the net sales of our convertible preferred stock and net proceeds of $19.8 million through borrowings under our loan and security agreement with Oxford Finance LLC, or the 2020 Credit Facility. We have also partnered one of our encapsulation technology programs with Lilly. Under the terms of the partnership, we received an upfront payment of $62.5 million and we are eligible to receive additional milestone payments of up to $165.0 million upon achievement of certain regulatory milestones and sales-based milestones of up to $250.0 million for SIG-002. We are also eligible to receive tiered royalty payments in the mid-single digit to low-double digit percentages based on certain sales thresholds. Finally, Lilly is obligated to reimburse us for costs incurred to perform the research and development activities for the first developed product candidate that exceed $47.5 million. We are also eligible to receive additional payments upon the achievement of specified regulatory and sales milestones and royalty payments. As of December 31, 2022, we had cash, cash equivalents and marketable securities of $69.6 million.

On April 14, 2022, we entered into an Equity Distribution Agreement with Canaccord Genuity LLC, or Canaccord, pursuant to which we may issue and sell shares of common stock, from time to time, having an aggregate offering price of up to $10.0 million. Sales of common stock through Canaccord may be made by any method that is deemed an "at the market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended. We are not obligated to make any sales of its common stock under the Equity Distribution Agreement. Any sales under the Equity Distribution Agreement will be made pursuant to our registration statement on Form S-3 (File No 333- 264296), which became effective on April 22, 2022 and the prospectus relating to such offering.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Net cash used in operating activities	$ (51,474)	$ (78,405)
Net cash used in investing activities	(12,081)	(18,060)
Net cash (used in) provided by financing activities	(1,606)	1,554
Net decrease in cash, cash equivalents and restricted cash	$ (65,161)	$ (94,911)

Operating Activities

During the year ended December 31, 2022, operating activities used $51.5 million of cash, primarily resulting from our net loss of $43.6 million and net cash used in changes in our operating assets and liabilities of $19.3 million, partially offset by non-cash charges of $11.4 million. Net changes in our operating assets and liabilities for the year ended December 31, 2022 consisted primarily of a $9.5 million decrease in deferred revenue, a $4.1 million decrease in lease liabilities, a $2.9 million decrease in accrued expenses and other current liabilities, a $2.1 million increase in accounts receivable, a $1.3 increase in unbilled accounts receivable, and $1.2 million decrease in accounts payable, offset by a decrease in prepaid expenses and other current assets of $1.7 million and a $0.2 million increase in other liabilities. The decrease in deferred revenue was due to recognition of revenue related to our collaboration agreement. The increase in accounts receivable and unbilled accounts receivable was due to work performed related to our collaboration agreement that was either not paid or not invoiced as of the year ended December 31, 2022. The decrease in accounts payable and accrued expenses and other current liabilities was the result of timing of payments for services performed by our vendors. The decrease in lease liabilities was primarily due to payment of rent for our leased property. The increases in prepaid expenses and other current assets were the result of timing of payments for services to be performed in future periods.

During the year ended December 31, 2021, operating activities used $78.4 million of cash, primarily resulting from our net loss of $77.3 million and net cash used in changes in our operating assets and liabilities of $13.4 million, partially offset by non-cash charges of $12.3 million. Net changes in our operating assets and liabilities for the year ended December 31, 2021 consisted primarily of a $9.4 million decrease in deferred revenue, a $4.7 million decrease in lease liabilities and a $1.0 million increase in prepaid expenses and other current assets, partially offset by a $0.9 million increase in accrued expenses and other current liabilities and a $0.7 million increase in accounts payable. The decrease in deferred revenue was due to recognition of revenue related to our collaboration agreement. The decrease in lease liabilities was primarily due to payment of rent for our leased property. The increase in accrued expenses and other current liabilities and accounts payable were primarily due to the timing of vendor invoicing and payments.

Investing Activities

During the year ended December 31, 2022, net cash used in investing activities was $12.1 million and consisted of $42.5 million in purchases of marketable securities, and $0.5 million in purchases of laboratory equipment and furniture and fixtures, offset by $30.8 million in proceeds from maturities of marketable securities and proceeds from the sale of fixed assets of $0.2 million.

During the year ended December 31, 2021, net cash used in investing activities was $18.1 million and consisted of $16.2 million in purchases of marketable securities and $1.8 million in purchases of laboratory equipment and furniture and fixtures.

Financing Activities

During the year ended December 31, 2022, net cash used in financing activities was $1.6 million, consisting primarily of $1.7 million in repayments of principal associated with our debt facility, offset by $0.1 million of the proceeds from our employee stock purchase plan.

During the year ended December 31, 2021, net cash provided by financing activities was $1.6 million, consisting primarily of the proceeds from the exercise of stock options of $2.2 million, which was partially offset by $0.6 million in the payment of issuance costs associated with our initial public offering in December 2020.

Loan and security agreement

In September 2020, the Company entered into a loan and security agreement, or the 2020 Credit Facility, with Oxford Finance LLC, or Oxford. Effective as of September 2020, the Company paid off in full its borrowings under our prior debt facility using part of the proceeds from the 2020 Credit Facility and accounted for this as a debt extinguishment. The 2020 Credit Facility initially provided for borrowings of up to $20.0 million under one term loan, or the Term A Loan, as well as additional borrowings of up to an aggregate of $5.0 million, under one additional term loan, or the Term B Loan, collectively the "Term Loans". Under the 2020 Credit Facility, the Company borrowed $20.0 million in September 2020. The Company did not elect to borrow the additional $5.0 million under the Term B Loan and the option to borrow under the Term B Loan has expired. Borrowings under the 2020 Credit Facility bear interest at an annual rate equal to greater of 8.40% and the sum of the thirty-day U.S. Dollar LIBOR rate report in the *Wall Street Journal* plus 8.23%, and are repayable in monthly interest only payments through August 2022 and in equal monthly payments of principal plus accrued interest from September 2022 until the maturity date in August 2025. Upon repayment of the Term Loans, the Company is required to make a final payment to Oxford equal to 3.5% of the original principal amount of the Term Loans funded which will be accrued by charges to interest expense over the term of the loans using the effective-interest method.

Borrowings under the 2020 Credit Facility are collateralized by substantially all of our personal property, other than our intellectual property. There are no financial covenants associated with the 2020 Credit Facility; however, we are subject to certain affirmative and negative covenants to which we will remain subject until maturity. These covenants include limitations on dispositions, mergers or acquisitions; encumbering our intellectual property; incurring indebtedness or liens; paying dividends; making certain investments; and engaging in certain other business transactions. In addition, we are required to, among other things, on an annual basis to deliver Oxford Finance LLC annual audited financial statements. Obligations under the 2020 Credit Facility are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in our business, operations or financial or other condition.

As of December 31, 2022 and 2021, the interest rate applicable to borrowings under the 2020 Credit Facility was 12.4% and 8.40%, respectively. During the year ended December 31, 2022 and 2021 the weighted average effective interest rate on outstanding borrowings was 13.8% and 9.8%.

As of December 31, 2022, we were in compliance with all debt covenants pursuant to the 2020 Credit Facility. We cannot be assured that we will be able to obtain additional covenant waivers or amendments in the future which may have a material adverse effect on our results or operations or liquidity.

Funding requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials for our product candidates in development. The timing and amount of our operating and capital expenditures will depend largely on:

- the costs of continuing to develop our SLTx platform, including the cost of any changes to our cells, spheres or manufacturing processes and the costs of any additional preclinical studies we may conduct;

- the costs of acquiring licenses for the components and engineered cell lines that will be used with our current and future product candidates;

- the scope, progress, results, and costs of discovery, preclinical development, formulation development, and clinical trials for our current and future product candidates;

- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims;

- the costs, timing, and outcome of regulatory review of any of our product candidates;

- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, distribution, coverage and reimbursement for any of our product candidates for which we receive regulatory approval;

- the cost of developing and expanding our manufacturing capabilities and advancing these manufacturing capabilities to manufacture product candidates that are commercially viable;

- our ability to establish and maintain additional collaborations on favorable terms, if at all;

- the success of any collaborations that we may establish and of our license agreements;

- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain; and

- the extent to which we acquire or in-license product candidates, intellectual property and technologies.

We believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements into 2025, giving effect to our decreased external spend relating to our MPS-1 program beginning in the first quarter of 2023. We have based this estimate on assumptions that may change, and we could utilize our available capital resources sooner than we expect.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends. If we raise additional funds through additional collaborations, strategic alliances or marketing, distribution 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 grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our research, product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK

We are a smaller reporting company, as defined by Rule 12b-2 of the Exchange Act, and are not required to provide this information.

Item 8. CONSOLIDATED FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

SIGILON THERAPEUTICS INC.
CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Sigilon Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Sigilon Therapeutics, Inc. and its subsidiary (the "Company") as of December 31, 2022 and 2021, and the related consolidated statements of operations and comprehensive loss, of stockholders' equity and of cash flows for the years then ended, including 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 as of December 31, 2022 and 2021, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated 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 of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated 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 consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 14, 2023

We have served as the Company's auditor since 2017.

SIGILON THERAPEUTICS, INC.
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 42,066	$ 107,143
Marketable securities	27,560	16,213
Accounts receivable	2,171	59
Unbilled accounts receivable	1,287	—
Prepaid expenses and other current assets	1,077	2,729
Restricted cash—current	250	250
Total current assets	74,411	126,394
Property and equipment, net	2,854	3,994
Right-of-use assets	8,979	12,863
Restricted cash	1,034	1,118
Total assets	$ 87,278	$ 144,369
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 936	$ 2,344
Accrued expenses and other current liabilities	6,021	8,998
Lease liabilities, current portion	4,485	4,845
Current portion of long-term debt	6,667	1,667
Deferred revenue from related party, current portion	12,885	17,034
Total current liabilities	30,994	34,888
Deferred revenue from related party, net of current portion	—	5,333
Lease liability, net of current portion	4,888	8,577
Long-term debt, net of discount and current portion	12,021	18,411
Other liabilities	233	—
Total liabilities	48,136	67,209
Commitments and contingencies (Note 12)		
Stockholders' equity		
Common stock, par value $0.001 per share; 175,000,000 shares authorized at December 31, 2022 and December 31, 2021; 32,466,737 and 32,359,895 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively	32	32
Preferred stock, par value $0.001 per share; 25,000,000 shares authorized at December 31, 2022 and December 31, 2021; no shares issued and outstanding at December 31, 2022 and December 31, 2021	—	—
Additional paid-in capital	296,339	290,377
Accumulated other comprehensive loss	(429)	(10)
Accumulated deficit	(256,800)	(213,239)
Total stockholders' equity	39,142	77,160
Total liabilities and stockholders' equity	$ 87,278	$ 144,369

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

SIGILON THERAPEUTICS, INC.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except per share data)

	Year Ended December 31,	
	2022	2021
Revenue		
Collaboration revenue	$ 12,944	$ 9,599
Operating expenses:		
Research and development	37,631	65,069
General and administrative	18,979	20,166
Total operating expenses	56,610	85,235
Loss from operations	(43,666)	(75,636)
Other income (expense), net:		
Interest income	946	258
Interest expense	(2,290)	(1,988)
Other income, net	1,449	55
Total other income (expense), net	105	(1,675)
Net loss attributable to ordinary shareholders	$ (43,561)	$ (77,311)
Net loss per share attributable to common stockholders—basic and diluted	$ (1.34)	$ (2.43)
Weighted average common stock outstanding—basic and diluted	32,405,786	31,860,264
Other comprehensive loss		
Unrealized loss on marketable debt securities	(419)	(10)
Total other comprehensive loss	(419)	(10)
Total comprehensive loss	$ (43,980)	$ (77,321)

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

SIGILON THERAPEUTICS, INC.
Consolidated Statements of Stockholders' Equity
(In thousands, except per share data)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balances at December 31, 2020	31,464,989	$ 31	$ 282,053	$ —	$ (135,928)	$ 146,156
Issuance of common stock upon exercise of stock options	878,015	1	2,094	—	—	2,095
Issuance of ESPP shares	16,891	—	81	—	—	81
Stock-based compensation expense	—	—	6,149	—	—	6,149
Unrealized loss on marketable debt securities	—	—	—	(10)	—	(10)
Net loss	—	—	—	—	(77,311)	(77,311)
Balances at December 31, 2021	32,359,895	32	290,377	(10)	(213,239)	77,160
Issuance of common stock upon exercise of stock options	833	—	1	—	—	1
Issuance of common stock upon vesting of restricted stock units	37,960	—	—	—	—	—
Issuance of ESPP shares	68,049	—	60	—	—	60
Stock-based compensation expense	—	—	5,901	—	—	5,901
Unrealized loss on marketable debt securities	—	—	—	(419)	—	(419)
Net loss	—	—	—	—	(43,561)	(43,561)
Balances at December 31, 2022	32,466,737	$ 32	$ 296,339	$ (429)	$ (256,800)	$ 39,142

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

SIGILON THERAPEUTICS, INC.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2022	2021
Cash flows from operating activities:		
Net loss	$ (43,561)	$ (77,311)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Depreciation and amortization expense	1,264	1,118
Gain on disposal of fixed assets	(48)	—
Stock-based compensation expense	5,901	6,149
Non-cash lease expense	3,952	4,785
Non-cash interest expense	277	271
Amortization of premium on marketable securities	8	3
Changes in operating assets and liabilities:		
Accounts receivable	(2,112)	118
Unbilled accounts receivable	(1,287)	—
Prepaid expenses and other current assets	1,652	(1,000)
Accounts payable	(1,236)	713
Accrued expenses and other current liabilities	(2,918)	908
Other liabilities	233	—
Lease liabilities	(4,117)	(4,749)
Deferred revenue	(9,482)	(9,410)
Net cash used in operating activities	(51,474)	(78,405)
Cash flows from investing activities:		
Purchases of marketable securities	(42,524)	(16,226)
Proceeds from maturities of marketable securities	30,750	—
Purchase of property and equipment	(537)	(1,834)
Proceed from the sale of fixed assets	230	—
Net cash used in investing activities	(12,081)	(18,060)
Cash flows from financing activities:		
Payments of deferred offering costs	—	(622)
Repayment of debt	(1,667)	—
Proceeds from the exercise of common stock options and employee equity plans	61	2,176
Net cash (used in) provided by financing activities	(1,606)	1,554
Net decrease in cash, cash equivalents and restricted cash	(65,161)	(94,911)
Cash, cash equivalents and restricted cash at beginning of period	108,511	203,422
Cash, cash equivalents and restricted cash at end of period	$ 43,350	$ 108,511
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 2,004	$ 1,710
Supplemental disclosures of noncash investing and financing activities:		
Right-of-use assets obtained in exchange for lease liabilities	$ 68	$ 917
Purchases of property and equipment included in accounts payable and accrued expenses	$ 91	$ 322

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

1. Nature of the Business and Basis of Presentation

Sigilon Therapeutics, Inc. (the "Company" or "Sigilon") is a preclinical stage biotechnology company pioneering a new class of therapeutics and seeking to develop functional cures for patients with acute and chronic diseases by providing stable and durable levels of therapeutic molecules to patients. The Company was incorporated on May 14, 2015 under the laws of the State of Delaware.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, the successful completion of research and development, development by competitors of new technological innovations, dependence on key personnel, protection of technology, compliance with government regulations, and the ability to secure additional capital to fund operations and commercial success of its product candidates. The Company is also subject to additional risks and uncertainties related to the ongoing COVID-19 pandemic and other macroeconomic and geopolitical events, which collectively have caused and may continue to cause major disruptions to businesses and economies worldwide.

Since its inception, the Company has devoted substantially all of its efforts to raising capital, obtaining financing, and incurring research and development costs related to advancing its biomedical platform. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-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.

Basis of Presentation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiary Sigilon Securities Corporation. All intercompany balances and transactions have been eliminated. The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP").

Going Concern

The Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date the financial statements are issued.

From its inception through December 31, 2022, the Company has funded its operations primarily with proceeds from its IPO, sales of convertible preferred stock, payments received under its collaboration agreement and proceeds from borrowings under loan and security agreements. The Company has incurred recurring losses since inception, including net losses of $43.6 million and $77.3 million for the years ended December 31, 2022 and 2021, respectively. In addition, as of December 31, 2022, the Company had an accumulated deficit of $256.8 million. The Company expects to generate significant losses and negative cash flows from operations for the foreseeable future.

Based on its current operating plans, the Company believes its cash, cash equivalents and marketable securities of $69.6 million as of December 31, 2022 will be sufficient to fund its anticipated level of operations, capital expenditures and satisfy debt repayments for a period of at least 12 months from the issuance date of this Annual Report. The Company expects to generate operating losses for the foreseeable future. Accordingly, the Company will seek additional funding through equity financings, debt financing, or additional collaboration agreements. If the Company is unable to raise additional funds through equity financing, debt financings or additional collaboration agreements the Company may be required to delay, limit, reduce or terminate product development or future commercialization efforts or grant rights to develop and market products or product candidates that the Company would otherwise prefer to develop and market itself.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the period. Estimates and assumptions reflected in these financial statements include, but are not limited to, revenue recognition, research and development expenses and stock-based awards. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates as there are changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results may differ from those estimates or assumptions.

Concentration of Credit Risk and of Significant Suppliers

The financial instruments that potentially subject the Company to concentrations of credit risk are cash, cash equivalents, marketable securities, and accounts receivable. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships. As of December 31, 2022, 100% of the Company's accounts receivable related to one customer and as of December 31, 2021, the Company's accounts receivable were related to two customers. As of December 31, 2022 and 2021, 100% and 39%, respectively, of the Company's account receivables were related to the Company's collaboration agreements with Eli Lilly and Company (Note 9).

The Company is dependent on third-party manufacturers to supply certain products for research and development activities in its programs. The Company currently has a supplier of certain raw materials that would be considered a sole supplier. If the Company cannot access additional suppliers or secure sufficient inventory of these raw materials, its programs could be adversely affected by an interruption in the availability of these raw materials.

Restricted Cash

In connection with the Company's corporate headquarters and lab space lease agreement entered into in March 2018, the Company is required to maintain a letter of credit of $0.6 million for the benefit of the landlord. On October 16, 2020 the Company took over the lease of office and laboratory space adjacent to its current headquarters, which expires in February 2025. Under the terms of the lease, the Company is required to maintain a letter of credit of $0.5 million. The Company has classified the certificate of deposits collateralizing the letter of credits issued as a security deposit in connection with the Company's leases of its corporate facility as long-term restricted cash on its balance sheet at December 31, 2022 and 2021. At December 31, 2022 and 2021 the Company classified $0.3 million related to securing the use of corporate credit cards as short-term restricted cash.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation and amortization expense is recognized using the straight-line method over the estimated useful life of each asset, as follows:

	Estimated useful life
Laboratory equipment	5 Years
Leasehold improvements	Shorter of the lease term or 10 years
Furniture and fixtures	7 Years
Computers and software	3 Years

Maintenance and repairs are charged to expense as incurred. Costs for capital assets not yet placed into service are capitalized as construction-in-progress and depreciated once placed into service. When assets are retired or otherwise disposed of, the cost of these assets and related accumulated depreciation or amortization are removed from the accounts

and any resulting gains or losses are included in the statement of operations and comprehensive loss in the period of disposal.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss to be recognized would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. The Company did not recognize any impairment losses on long-lived assets during the years ended December 31, 2022 and 2021.

Leases

The Company follows the provisions of ASC Topic 842, *Leases* ("ASC 842"), for all contracts and agreements that are within its scope. Under ASC 842, 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 in the arrangement, including whether the Company controls the use of identified assets. The Company classifies leases with a term greater than one year as either operating or finance leases at the lease commencement date and records a right-of-use assets and current and non-current lease liabilities, as applicable on the balance sheet. The Company has elected not to recognize on the balance sheet leases with terms of one year or less, but payments are recognized as expense on a straight-line basis over the lease term. If a lease includes options to extend the lease term, the Company does not assume the option will be exercised in its initial lease term assessment unless there is reasonable certainty that the Company will renew based on an assessment of economic factors present as of the lease commencement date. The Company monitors its plans to renew its material leases each reporting period.

Lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the remaining lease term. The present value of future lease payments are discounted using the interest rate implicit in lease contracts if that rate is readily determinable; otherwise the Company utilizes its incremental borrowing rate ("IBR"), which reflects the fixed rate at which the Company could borrow on a collateralized basis over a similar term, the amount of the lease payments in a similar economic environment. After lease commencement and the establishment of a right-to-use asset and operating lease liability, lease expense is recorded on a straight-line basis over the lease term.

The Company enters into contracts that contain both lease and non-lease components. Non-lease components include costs that do not provide a right-to-use a leased asset but instead provide a service, such as maintenance costs. The Company has elected to account for the lease and non-lease components together as a single component for all classes of underlying assets. Variable costs associated with the lease, such as maintenance and utilities, are not included in the measurement of right-to-use assets and lease liabilities but rather are expensed when the events determining the amount of variable consideration to be paid have occurred.

Fair Value Measurements

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable

inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

Level 1 — Quoted prices in active markets for identical assets or liabilities.
Level 2 — Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The carrying values of the Company's accounts receivable, and accounts payable and accrued expenses and other current liabilities approximate their fair value due to the short-term nature of these assets and liabilities. The carrying value of the Company's long-term debt approximates its fair value at December 31, 2022 because the debt bears interest at a variable market rate and the Company's credit risk has not materially changed since the inception of the agreement. The Company's financial instruments consist primarily of cash, cash equivalents and marketable securities (Note 3).

Segment Information

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company is developing therapeutic treatments for a wide range of chronic diseases. The Company has determined that its chief operating decision maker is its Chief Executive Officer. The Company's chief operating decision maker reviews the Company's financial information on an aggregated basis for purposes of allocating resources and assessing financial performance. All the Company's tangible assets are located in the United States and all of the Company's collaboration revenue is derived from its collaboration partners headquartered in the United States.

Cash and cash equivalents

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at the date of acquisition to be cash equivalents.

Marketable securities

Marketable securities consist of investments with original maturities greater than ninety days. The Company has classified its investments with maturities beyond one year as short term, based on their highly liquid nature and because such marketable securities represent the investment of cash that is available for current operations. The Company considers its investment portfolio of investments as available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Unrealized gains and losses are reported as a component of accumulated other comprehensive loss in stockholders' equity. Realized gains and losses and declines in value judged to be other than temporary are included as a component of other income (expense), net based on the specific identification method. When determining whether a decline in value is other than temporary, the Company considers various factors, including whether the Company has the intent to sell the security, and whether it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis. Fair value is determined based on quoted market prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

Revenue Recognition for License and Collaboration Agreements

The Company follows the provisions of ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606"), for all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments.

Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the Company expects to receive in exchange for those goods or

services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when, or as, the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract, determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company enters into licensing arrangements that are within the scope of ASC 606, under which it may exclusively license to third parties' rights to develop, manufacture and commercialize its product candidates. The terms of these arrangements typically include payment to the Company of one or more of the following: nonrefundable, upfront license fees; reimbursement of research and development costs; development, regulatory and sales milestone payments; and royalties on net sales of licensed products. For costs that were not paid upfront, the payment terms under the Company's existing licensing arrangements are generally 45 days.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under its arrangements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the assessment of the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations, and (v) recognition of revenue when, or as, the Company satisfies each performance obligation. As part of the accounting for arrangements under ASC 606, the Company must use significant judgment to determine: a) the performance obligations based on the determination under step (ii) above; b) the transaction price under step (iii) above; and c) the standalone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. The Company also uses judgment to determine whether milestones or other variable consideration, except for royalties and sales-based milestones, should be included in the transaction price as described below. The transaction price is allocated to each performance obligation based on the relative stand-alone selling price of each performance obligation in the contract, and the Company recognizes revenue based on those amounts when, or as, the performance obligations under the contract are satisfied.

The standalone selling price is the price at which an entity would sell a promised good or service separately to a customer. Management estimates the standalone selling price of each of the identified performance obligations in the Company's customer contracts, maximizing the use of observable inputs. Because the Company has not sold the same goods or services in its contracts separately to any customers on a standalone basis and there are no similar observable transactions in the marketplace, the Company estimates the standalone selling price of each performance obligation in its customer arrangements based on its estimate of costs to be incurred to fulfil its obligations associated with the performance, plus a reasonable margin.

The Company has determined that its only contract liability under ASC 606 is deferred revenue. Amounts received prior to revenue recognition are recorded as deferred revenue in the balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as the current portion of deferred revenue in the balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion in the balance sheets. Amounts are recorded as accounts receivable and unbilled accounts receivable when the Company's right to consideration is unconditional.

Exclusive Licenses

If the license granted in the arrangement is determined to be distinct from the other promises or performance obligations identified in the arrangement, which generally include research and development services, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a license is distinct from the

other promises, the Company considers relevant facts and circumstances of each arrangement, including the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining promises, whether the value of the license is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises, and whether it is separately identifiable from the remaining promises. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and the resulting periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the arrangement. Such a change could have a material impact on the amount of revenue the Company records in future periods. Under the Company's existing license and collaboration agreement, the Company has concluded the research and development services and the license, among other promises are a combined performance obligation (Note 9) and that the transfer of control to the customer occurs over the time period that the research and development services are to be provided by the Company, and this cost-to-cost method is, in management's judgement, the best measure of progress towards satisfying the performance obligation.

Research and Development Services

The promises under the Company's collaboration and license agreements generally include research and development services to be performed by the Company on behalf of the collaboration partner. Payments or reimbursements resulting from the Company's research and development efforts are estimated at the outset of the arrangement and considered part of the transaction price that is subsequently recognized as revenue because the Company is the principal in the arrangement for such efforts.

Customer Options

The Company's arrangements may provide a customer with the right to certain optional purchases, such as the right to license a target either at the inception of the arrangement or within a predefined option period. Under these agreements, fees may be due to the Company at the inception of the arrangement as an upfront fee or payment or upon the exercise of an option to acquire a license. If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the Company evaluates the customer options to determine if they are material rights at the outset of each arrangement. If the goods and services underlying the customer options are not determined to be material rights, these customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon exercise of the option. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the relative stand-alone selling price, which is determined based on the identified discount, and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised or expires.

Milestone Payments

At the inception of each arrangement that includes research, development or regulatory milestone payments, we evaluate whether the milestones are considered likely to be met and estimate the amount to be considered for inclusion in the transaction price using the most-likely-amount method. If it is probable that a significant reversal in the amount of cumulative revenue recognized would not occur, the associated milestone value is included in the transaction price. For milestone payments due upon events that are not within the control of us or the licensee, such as regulatory approvals, we are not able to assert that it is likely that the regulatory approval will be granted and that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur until those approvals are received. In making this assessment, we evaluate factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone. There is considerable judgment involved in determining whether it is probable that a significant reversal in the amount of cumulative revenue recognized would not occur. At the end of each subsequent reporting period we reevaluate the probability of achievement of all milestones subject to constraint and, if

necessary, adjust our estimate of the overall transaction price of the arrangement. Any such adjustments are recorded on a cumulative catch-up basis, which would affect the amount of revenue and earnings in the period of adjustment. As of December 31, 2022 and 2021, no milestones under the 2018 Lilly Agreement (Note 9) were included in the transaction price as no milestones had been deemed likely to be achieved or had been achieved.

Royalties

For arrangements that include sales-based royalties, including milestone payments based on a level of sales, that are the result of a customer-vendor relationship and for which the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied or partially satisfied. To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including costs for salaries and bonuses, employee benefits, subcontractors, facility-related expenses, depreciation and amortization, stock-based compensation, third-party license fees, laboratory supplies, and external costs of outside vendors engaged to conduct discovery, preclinical and clinical development activities and clinical trials as well as to manufacture clinical trial materials, and other costs. The Company recognizes external research and development costs based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its service providers.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such prepaid expenses are recognized as an expense when the goods have been delivered or the related services have been performed, or when it is no longer expected that the goods will be delivered, or the services rendered.

Upfront payments under license agreements are expensed as research and development expense upon receipt of the license, and annual maintenance fees under license agreements are expensed in the period in which they are incurred. Milestone payments under license agreements are accrued, with a corresponding expense being recognized, in the period in which the milestone is determined to be probable of achievement and the related amount is reasonably estimable.

Research, Development and Manufacturing Contract Costs and Accruals

The Company has entered into various research, development and manufacturing contracts with research institutions and other companies. These agreements are generally cancelable, and related costs are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research, development and manufacturing costs. When billing terms under these contracts do not coincide with the timing of when the work is performed, the Company is required to make estimates of outstanding obligations to those third parties as of period end. Any accrual estimates are based on a number of factors, including the Company's knowledge of the progress towards completion of the research, development and manufacturing activities, invoicing to date under the contracts, communication from the research institutions and other companies of any actual costs incurred during the period that have not yet been invoiced and the costs included in the contracts. Significant judgments and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the estimates made by the Company. The historical accrual estimates made by the Company have not been materially different from the actual costs.

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

We measure stock-based awards granted to employees, non-employees and directors based on the fair value on the date of the grant and recognize compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. Forfeitures are accounted for as they occur. Generally, we issue stock-based awards in the form of stock options and restricted stock units with only service-based vesting conditions and record the expense for these awards using the straight-line method. We have also issued stock-based awards with performance-based vesting conditions for which the expense is recognized when achievement of such performance conditions becomes probable.

The fair value of each share option is estimated on the date of grant using the Black-Scholes option pricing model. Until the completion of our initial public offering in December 2020, we had been a private company and lacked company-specific historical and implied volatility information for our shares. Therefore, we estimate our expected share price volatility based on the historical volatility of publicly traded peer companies and expect to continue to do so until such time as we have adequate historical data regarding the volatility of our own traded share price. The expected term of our share options has been determined utilizing the "simplified method" for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that we have never paid cash dividends on our ordinary shares and do not expect to pay any cash dividends in the future.

The Company classifies stock-based compensation expense in its statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements or in the Company's tax returns. Deferred taxes are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect in the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Comprehensive Loss

Comprehensive loss is composed of net loss and other comprehensive loss. Other comprehensive loss consists of unrealized losses on marketable securities.

Net Income (Loss) per Share

The Company only has one class of shares outstanding and basic net income (loss) per common share is computed by dividing the net income (loss) by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) per common share is computed by dividing net income (loss) by the weighted average number of shares of common stock outstanding for the period, including potential dilutive common shares assuming the dilutive effect of outstanding stock awards. For periods in which the Company reports a net loss, diluted net loss per common share is the same as basic net loss per common share, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Recently Issued Accounting Pronouncements

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments—Credit Losses (Topic 362): Measurement of Credit Losses on Financial Statements* ("ASU 2016-13"). The new standard requires that expected credit losses relating to financial assets measured on an amortized cost basis and available-for-sale debt securities be recorded through an allowance for credit losses. It also limits the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and also requires the reversal of previously recognized credit losses if fair value increases. The targeted transition relief standard allows filers an option to irrevocably elect the fair value option of ASC 825-10, *Financial Instruments-Overall*, applied on an instrument-by-instrument basis for eligible instruments. The Company adopted ASU 2016-13 on January 1, 2022 and the adoption of this standard did not have a material impact on its financial statements.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The new standard will be effective for public business entities, for fiscal years beginning after December 15, 2020, and for all other entities, for fiscal years beginning after December 15, 2021 and the Company adopted ASU 2016-13 on January 1, 2022. The adoption of ASU 2019-12 did not have a material impact on the Company's financial statements.

In March 2020, the FASB issued ASU No. 2020-04, *Reference Rate Reform (Topic 848): Facilitation of the Effects of Reference Rate Reform on Financial Reporting* ("ASU 2020-04"), which provide optional expedients and exceptions for applying generally accepted accounting principles to contracts, hedging relationships, and other transactions that reference the London Interbank Offered Rate ("LIBOR") or another reference rate expected to be discontinued because of reference rate reform if contract modifications are made on or before December 31, 2022. The amendments in this update are effective for all entities as of March 12, 2020 and do not apply to contract modifications made, and hedging relationships entered into or evaluated, after December 31, 2022. The adoption of ASU 2020-04 did not have a material impact on the Company's financial statements.

3. Fair Value Measurements

Value Measurements

The following tables present information about the Company's financial assets that have been measured at fair value as of December 31, 2022 and indicate the fair value of the hierarchy of the valuation inputs utilized to determine such fair value. In general, fair values determined by Level 1 inputs utilize quoted prices (unadjusted) in active markets for identical assets or liabilities. Fair value determined by Level 2 inputs utilize observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted market prices in markets that are not active or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or

liabilities. Fair values determined by Level 3 inputs are unobservable data points for the asset or liability, and include situations where there is little, if any, market activity for the asset or liability. During the years ended December 31, 2022 and 2021, there were no transfers between Level 1, Level 2 and Level 3.

The following table summarizes the Company's cash equivalents and marketable securities as of December 31, 2022 and 2021 (in thousands):

	Fair value measurements as of December 31, 2022			
	Level 1	Level 2	Level 3	Total
Cash equivalents				
Money market funds	$ 29,310	$ —	$ —	$ 29,310
Commercial paper	—	1,994	—	1,994
U.S. Treasuries	—	4,999	—	4,999
Total cash equivalents	29,310	6,993	—	36,303
Marketable securities				
Corporate bonds	—	21,594	—	21,594
Commercial paper	—	1,738	—	1,738
U.S. Government Agencies	—	1,235	—	1,235
U.S. Treasuries	—	2,993	—	2,993
Total marketable securities	—	27,560	—	27,560
Total	$ 29,310	$ 34,553	$ —	$ 63,863

	Fair value measurements as of December 31, 2021			
	Level 1	Level 2	Level 3	Total
Cash equivalents				
Money market funds	$ 50,847	$ —	$ —	$ 50,847
Commercial paper	—	25,995	—	25,995
Corporate bonds	—	1,000	—	1,000
Total cash equivalents	50,847	26,995	—	77,842
Marketable securities				
Corporate bonds	—	10,238	—	10,238
Commercial paper	—	5,975	—	5,975
Total marketable securities	—	16,213	—	16,213
Total	$ 50,847	$ 43,208	$ —	$ 94,055

Marketable Securities

The following tables summarizes the Company's available-for-sale marketable debt securities as of December 31, 2022 and 2021 (in thousands):

	Fair value measurements as of December 31, 2022				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Credit Losses	Total
Corporate bonds	$ 21,994	$ —	$ (400)	$ —	$ 21,594
Commercial paper	1,743	—	(5)	—	1,738
U.S. Treasuries	1,248	—	(13)	—	1,235
U.S. Government Agencies	2,999	—	(6)	—	2,993
Total	$ 27,984	$ —	$ (424)	$ —	$ 27,560

	Fair value measurements as of December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Total
Commercial paper	$ 10,244	$ —	$ (6)	$ 10,238
Corporate bonds	5,977	—	(2)	5,975
Total	$ 16,221	$ —	$ (8)	$ 16,213

The unrealized losses at December 31, 2022 were attributed to changes in interest rates and unrealized losses do not represent credit losses. No declines in value were deemed to be other than temporary as of December 31, 2021.

The following table summarizes the Company's available-for-sale marketable debt securities by contractual maturity, as of December 31, 2022 and 2021 (in thousands):

	December 31, 2022	December 31, 2021
Maturities in one year or less	$ 23,231	$ 9,004
Maturities between one and two years	4,329	7,209
Total	$ 27,560	$ 16,213

4. Property and Equipment, Net

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

	December 31, 2022	December 31, 2021
Laboratory equipment	$ 6,301	$ 6,297
Leasehold improvements	78	78
Furniture and fixtures	620	620
Computers and software	177	163
	7,176	7,158
Less: Accumulated depreciation and amortization	(4,322)	(3,164)
Total property and equipment, net	$ 2,854	$ 3,994

Depreciation and amortization expense for the years ended December 31, 2022 and 2021 was $1.3 million, and $1.1 million, respectively.

5. Accrued Expenses and Other Current Liabilities

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

	December 31, 2022	December 31, 2021
Employee compensation and benefits	$ 4,243	$ 3,071
External research and development costs	817	5,056
Legal and professional fees	714	656
Other	247	215
Total accrued expenses and other current liabilities	$ 6,021	$ 8,998

6. Debt

As of December 31, 2022 and 2021, long-term debt consisted of the following (in thousands):

	December 31, 2022	December 31, 2021
Principal amount of long-term debt	$ 18,333	$ 20,000
Less: Current portion of long-term debt	(6,667)	(1,667)
Long-term debt, net of current portion	11,666	18,333
Final debt payment liability	700	700
Debt discount, net of accretion	(345)	(622)
Long-term debt, net of discount and current portion	$ 12,021	$ 18,411

In September 2020, the Company entered into a loan and security agreement (the "2020 Credit Facility"), with Oxford Finance LLC ("Oxford"). Effective as of September 2020, the Company paid off in full its borrowings under our prior debt facility using part of the proceeds from the 2020 Credit Facility and accounted for this as a debt extinguishment. The 2020 Credit Facility initially provided for borrowings of up to $20.0 million under one term loan ("Term A Loan"), as well as additional borrowings of up to an aggregate maximum of $5.0 million, under one additional term loan ("Term B Loan") (collectively the "Term Loans"). Under the 2020 Credit Facility, the Company borrowed $20.0 million in September 2020. The Company did not elect to borrow the additional $5.0 million under the Term B Loan and the option to borrow under the Term B Loan has expired. Borrowings under the 2020 Credit Facility bear interest at an annual rate equal to greater of 8.40% and the sum of the thirty day U.S. Dollar LIBOR rate report in the *Wall Street Journal* plus 8.23%, and are repayable in monthly interest-only payments through August 2022 and in equal monthly payments of principal plus accrued interest from September 2022 until the maturity date in August 2025. Upon repayment of the Term Loans, the Company is required to make a final payment to Oxford equal to 3.5% of the original principal amount of the Term Loans funded which will be accrued by charges to interest expense over the term of the loans using the effective-interest method. The Company recorded $0.3 million of initial debt issuance costs as well as a discount on the final payment liability of $0.7 million as a reduction of the carrying amount of the 2020 Credit Facility. The Company recorded amortization of debt issuance costs and accretion of the final payment liability associated with the 2020 Credit Facility for a combined amount of $0.3 million included in interest expense for the year ended December 31, 2022 and 2021. As of December 31, 2022, the Company was in compliance with all financial covenants pursuant to the 2020 Credit Facility.

Borrowings under the 2020 Credit Facility are collateralized by substantially all of the Company's personal property, other than its intellectual property. The Company is subject to certain affirmative and negative covenants restricting the Company's activities, including limitations on dispositions, mergers or acquisitions; encumbering its intellectual property; incurring indebtedness or liens; paying dividends; making certain investments; and engaging in certain other business transactions. In addition, the Company is required, on an annual basis, to deliver to Oxford annual audited financial statements with an audit opinion from its independent registered public accounting firm. The obligations under the 2020 Credit Facility are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in the Company's business, operations or financial or other condition.

As of December 31, 2022 and 2021, the interest rate applicable to borrowings under the 2020 Credit Facility was 12.4% and 8.40%, respectively, and the weighted average effective interest rate on outstanding borrowings was approximately 13.8% and 9.80%, respectively.

The estimated future principal payments due were as follows (in thousands):

	December 31, 2022
2023	$ 6,666
2024	6,667
2025	5,000
2026	—
2027	—
	$ 18,333

In connection with the 2020 Credit Facility, the Company issued to Oxford warrants to purchase up to 50,000 shares of Series B, convertible preferred stock, at an exercise price of $6.00 per share, which were immediately exercisable upon issuance. Following the issuance of the Series B-1 convertible preferred stock, the Series B warrants converted into Series B-1 warrants. Further, in conjunction with the completion of the IPO all warrants converted into warrants to acquire common stock. Following the Company's reverse stock split and the IPO there were 19,044 warrants to purchase Common Stock at an exercise price of $15.75. As of December 31, 2022 and 2021, 19,044 warrants to purchase Common Stock were outstanding and were classified as equity.

7. Common Stock

As of December 31, 2022 and 2021, the Company's Certificate of Incorporation, as amended and restated at such time, authorized the Company to issue 175,000,000 shares, of $0.001 par value common stock. Under the Company's certificate of incorporation, each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the Company's board of directors, if any, subject to the preferential dividend rights of the Preferred Stock. As of December 31, 2022 and 2021, no dividends had been declared.

At-the-Market Offering

On April 14, 2022, the Company entered into an Equity Distribution Agreement with Canaccord Genuity LLC, or Canaccord, pursuant to which the Company may issue and sell shares of common stock, from time to time, having an aggregate offering price of up to $10.0 million. Sales of common stock through Canaccord may be made by any method that is deemed an "at the market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended. The Company is not obligated to make any sales of its common stock under the Equity Distribution Agreement. Any sales under the Equity Distribution Agreement will be made pursuant to the registration statement on Form S-3 (File No 333- 264296), which became effective on April 22, 2022 and the prospectus relating to such offering. There were no sales under the Equity Distribution Agreement as of December 31, 2022.

8. Stock Based Compensation

Summary of Plans

In November 2020 the Company adopted the 2020 Incentive Plan (the "2020 Plan") and the 2020 Employee Stock Purchase Plan (the "2020 ESPP"). In 2016, the Company adopted the 2016 Equity Incentive Plan (the "2016 Plan"). These plans are administered by the Board of Directors or, at the discretion of the Board of Directors, by a committee of the Board of Directors.

2020 Incentive Plan

The 2020 Plan provides for the grant of stock options, stock appreciation rights, restricted stock awards, restricted stock units, unrestricted stock awards, performance-share awards, cash-based awards and dividend equivalent rights to employees, members of the board of directors and consultants of the Company. The number of shares initially reserved for issuance under the 2020 Plan was 1,500,000 shares of common stock. The number of shares reserved for issuance may

be increased by the number of shares under the previously authorized 2016 Stock Option Plan that are not needed to fulfill the Company's obligations for awards issued under the 2016 Stock Option Plan as a result of forfeiture, expiration, cancellation, termination or net issuances of awards thereunder. The number of shares of common stock that may be issued under the 2020 Plan is also subject to increase on the first day of each fiscal year by the lesser of (i) four percent of the Company's outstanding shares of common stock as of that date, or (ii) an amount determined by the board of directors. As of December 31, 2022, 1,850,378 shares were available for grant under the 2020 Plan.

The terms of stock awards agreements, including type of stock award to be granted, the provisions of each stock award, including the number of shares, vesting requirements and exercise prices, are determined by the board of directors and are subject to the provisions of the Plan. Option awards generally vest over a four-year period and expire after ten years. Certain options provide for accelerated vesting in the event of a change in control, as defined. The exercise price per share for stock options granted may not be less than the fair market value of the common stock at the date of grant.

2020 Employee Stock Purchase Plan

The 2020 ESPP provides participating employees with the opportunity to purchase shares of the Company's common stock at defined purchase prices over six-month offering periods. A total of 300,000 shares of common stock were initially reserved for issuance under this plan. The number of shares of common stock that may be issued under the 2020 ESPP will automatically increase on the first day of each calendar year, beginning on January 1, 2021 and ending on and including January 1, 2030, equal to the lesser of (i) 1% of the shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as determined by the board of directors, provided that not more than 3,200,000 shares of common stock may be issued under the 2020 ESPP. As of December 31, 2022, 853,307 shares were available for grant under the 2020 Plan. For the years ended December 31, 2022 and 2021, 68,049 and 16,891 shares of common stock were issued under the 2020 ESPP, respectively.

2016 Equity Incentive Plan

The 2016 Plan provided for the Company to grant incentive stock options and nonqualified stock options or other awards including restricted stock awards, unrestricted stock awards, and restricted stock units to the Company's employees, officers, directors, advisors, and consultants of the Company. No additional shares are to be granted under the 2016 Plan. Shares that are expired, terminated, surrendered, or canceled without having been fully exercised will be available for future awards under the 2020 Plan.

The terms of stock awards agreements, including type of stock award to be granted, the provisions of each stock award, including the number of shares, vesting requirements and exercise prices, were determined by the board of directors and are subject to the provisions of the Plan. Option awards generally vest over a four-year period and expire after ten years. Certain options provide for accelerated vesting in the event of a change in control, as defined. The exercise price per share for stock options granted may not be less than the fair market value of the common stock at the date of grant.

Stock Option Valuation

The fair value of each option is estimated on the date of grant using the Black-Scholes option-pricing model. The Company was a private company prior to the initial public offering and lacked company-specific historical and implied volatility information for its stock. Therefore, it estimates its expected stock price volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected term of options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield of 0% is based on the fact that the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future.

The following table presents, on a weighted average basis, the assumptions used in the Black-Scholes option-pricing model to determine the grant-date fair value of stock options granted to employees and directors:

	Year ended December 31,	
	2022	2021
Risk-free interest rate	1.75 %	0.80 %
Expected dividend yield	0.00 %	0.00 %
Expected term (in years)	6.0	6.1
Expected volatility	84.28 %	78.31 %

Stock Option Activity

The following table summarizes the Company's stock option activity since December 31, 2021:

	Number of options	Weighted average exercise price	Weighted average remaining contractual term (in years)	Aggregate intrinsic value (in thousands)
Balances at December 31, 2021	3,138,646	$ 10.74	7.6	$ 328
Options granted	2,564,140	2.23		
Options cancelled	(789,567)	8.64		
Options exercised	(833)	0.57		
Outstanding and expected to vest at December 31, 2022	4,912,386	6.63	7.8	—
Exercisable at December 31, 2022	2,045,196	$ 7.81	6.1	$ —

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those options that had exercise prices lower than the fair value of the Company's common stock.

The aggregate intrinsic value of stock options exercised during the twelve months ended December 31, 2022 and 2021 were less than $0.1 million and $6.0 million, respectively. The weighted average grant date fair value of stock options during the years ended December 31, 2022 and 2021 was $1.58 and $19.00, respectively.

Restricted Stock Units

The Company has granted restricted stock units with time-based vesting conditions to employees. The restricted stock units primarily vest over 3 years from the grant date. The Company values restricted stock units on the grant-date using the market price of the Company's common stock.

The following table summarizes restricted stock unit activity since December 31, 2021:

	Shares	Weighted average grant date fair value
Unvested shares as of December 31, 2021	275,400	$ 5.57
Vested	(37,960)	5.55
Forfeited	(87,040)	5.62
Unvested shares as of December 31, 2022	150,400	$ 5.54

Stock-based Compensation Expense

Stock-based compensation expense related to stock options and restricted stock units was classified in the statement of operations and comprehensive loss as follows (in thousands):

	Year ended December 31,	
	2022	2021
Research and development	$ 1,883	$ 2,230
General and administrative	4,018	3,920
	$ 5,901	$ 6,150

As of December 31, 2022, total unrecognized stock-based compensation expense related to unvested stock-based awards was $10.4 million, which is expected to be recognized over a weighted average period of 2.0 years.

9. License and Collaboration Agreement

Lilly License and Collaboration Agreement

On April 2, 2018, the Company entered into a License and Collaboration Agreement with Lilly (the "2018 Lilly Agreement"). Under the 2018 Lilly Agreement, the Company granted Lilly an exclusive worldwide, royalty-bearing license, including the right to grant sublicenses, to the Company's encapsulation technology applied to islet cells. The Company is responsible for research and development activities, including supply and manufacturing activities, through investigational new drug ("IND") filing readiness for the first product candidate, including costs up to $47.5 million and certain supply and manufacturing of products and materials in Phase 1 clinical trials and for clinical and commercial use following Phase 1 clinical trials. Lilly will be responsible for development and commercialization of any licensed product post-IND filing readiness and research and development costs for the IND product candidate above the $47.5 million cost threshold. Lilly is also responsible for all research, development and commercialization related to any subsequent product candidate. The parties are collaborating with the intent of developing encapsulated cell therapies for the potential treatment of type 1 diabetes. The activities under the agreement are governed by a joint research committee ("JRC"), which meets quarterly and consists of at least three members each from the Company and Lilly.

Under the 2018 Lilly Agreement, Lilly was obligated to pay the Company a one-time, non-refundable and non-creditable license issuance fee of $62.5 million. Lilly is also obligated to make aggregate milestone payments to the Company of up to $165.0 million upon achievement of certain regulatory milestones for the first licensed product and regulatory milestones up to $160.0 million for additional licensed products. Lilly is also obligated to pay the company sales-based milestones of up to $250.0 million for each licensed product and tiered (from mid-single-to-low-double digit) sales-based royalties for each licensed product. The 2018 Lilly Agreement will expire upon the expiration of the last royalty term, on a product-by-product and country-for country basis. The royalty term, by product and country, commences upon the first commercial sale and ends upon the later to occur of (i) the expiration of the Company's patent rights of a product candidate developed under the Lilly Agreement, (ii) the expiration of any data exclusivity period in a country or (iii) 10 years after the first commercial sale.

The Company will have the right, and the obligation, to supply Lilly's requirements for the material to be used in the manufacture of licensed products for clinical and commercial use. In connection with the supply responsibilities, the parties may enter into supply and quality agreements for both clinical and commercial supply.

The Company evaluated the 2018 Lilly Agreement under ASC 606 as the transactions underlying the agreement were considered transactions with a customer. The Company identified the following material promises under the arrangement: (i) exclusive license to research, develop, manufacture and commercialize licensed products, (ii) initial technology transfer, (iii) research activities (including pre-IND supply), (iv) cell line development and supply, (v) product trademark election, (vi) requirement to supply Lilly with the licensed product related to Phase 1 clinical trial ("Phase 1 Supply") and (vii) participation in the JRC.

The Company determined that the exclusive license to research, develop, manufacture and commercialize the licensed product was not distinct from the related research and manufacturing activities to be provided by the Company as a result of Lilly being unable to benefit on its own or with other resources reasonably available in the marketplace because the license to the Company's intellectual property requires significant specialized capabilities in order to be further developed, the research services necessary to develop the product are highly specialized and the Company's proprietary technology is a key capability of that development. The cell line development and supply and research activities were determined not to be distinct because they are performed in conjunction with the research activities to further develop the underlying technology. The product trademark was determined not to be distinct because the benefit that Lilly receives from the Company's trademark license only exists when combined with the right to commercialize the licensed product. In addition, the Company determined that the impact of the participation in the JRC was insignificant and had an immaterial impact on the accounting model. Therefore, the Company determined that the first five promises should be combined into a single performance obligation (the "Combined Performance Obligation"). The Company determined the sixth promise, the Phase 1 Supply promise, is distinct in the contract. As this is at no cost to Lilly, the right to receive this supply represents a material right and a distinct performance obligation. As such, the Company determined there were two distinct performance obligations at the outset of the 2018 Lilly Agreement.

The Company determined that the $62.5 million upfront payment represents the entirety of the consideration to be included in the transaction price as of the outset of the arrangement. The potential milestone payments that the Company may have been eligible to receive were initially excluded from the transaction price at the outset of the arrangement because (i) all development and regulatory milestone payments did not meet the criteria for inclusion using the most-likely-amount method and (ii) the Company recognizes as revenue sales-based milestones and royalties when the related sales occur. As of December 31, 2022 and 2021 no milestones or royalties have been deemed likely to be achieved or have been achieved.

The Company recognizes revenue for the Combined Performance Obligation as the research, development and manufacturing services are provided using an input method, based on the cumulative costs incurred compared to the total estimated costs expected to be incurred to satisfy the Combined Performance Obligation. The transfer of control to the customer occurs over the time period that the research and development services are to be provided by the Company, and this cost-to-cost method is, in management's judgement, the best measure of progress toward satisfying this performance obligation. The Company allocated $56.6 million of the transaction price to the Combined Performance Obligation at the outset of the arrangement.

The Phase 1 Supply was determined to be a material right, and the standalone selling price was estimated using the expected cost-plus margin approach. The Company allocated $5.9 million of the transaction price to the Phase 1 Supply at the outset of the arrangement. The Company has determined that the Phase 1 Supply will be satisfied at a point in time when the customer obtains control of each unit of product. Therefore, the Company will recognize revenue as shipments of the Phase 1 Supply are made to Lilly.

The Company reevaluates the transaction price and the total estimated costs expected to be incurred to satisfy the performance obligations at the end of each reporting period and as uncertain events, such as changes to the expected timing and cost of certain research, development and manufacturing activities that the Company is responsible for, are resolved or other changes in circumstances occur, and, if necessary, the Company will adjust its estimate of the transaction price and total estimated costs expected to be incurred.

During the year ended December 31, 2022, consistent with the Company's presentation to the JRC, the Company revised its estimate of total costs to complete the activities under the 2018 Lilly Agreement to reflect the Company's experiences to date and the impact this has on its expected future research and development activities to satisfy the Combined Performance Obligation. During the year ended December 31, 2022, there has been an increase to the total estimated costs expected to be incurred of $13.5 million verse the estimate as of December 31, 2021. The increase in total estimated costs impacted both the Company's estimated transaction price for the 2018 Lilly Agreement, as Lilly is obligated to reimburse the Company if the costs exceed $47.5 million to complete the services, and the Company's input method used to recognize revenue, as this measure compares the Company's cumulative costs incurred to the Company's total estimated costs expected to be incurred. During the year ended December 31, 2022, based on the allocation of total transaction price to each performance obligation using the relative stand-alone selling price of each performance obligation

under the 2018 Lilly Agreement, the transaction price for the Combined Performance Obligation increased by $12.7 million and the Phase 1 supply performance obligation increased by $1.3 million.

During the years ended December 31, 2022 and 2021, the Company recognized $12.9 million and $9.6 million, respectively, of collaboration revenue. As of December 31, 2022 and 2021, the Company recorded as a contract liability deferred revenue of $12.9 million and $22.4 million, respectively, of which, $12.9 million and $17.0 million, respectively, were current liabilities in the accompanying balance sheet. As of both December 31, 2022 and 2021 the research and development services related to the Combined Performance Obligation were expected to be performed over a remaining period of approximately 2.0 years.

Contract Liability

The changes in the total contract liability (deferred revenue) balances related to the Company's license and collaboration agreements with Lilly were as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Deferred revenues at beginning of period	$ 22,367	$ 31,777
Revenues deferred during the period	3,458	—
Revenues recognized during the period	(12,940)	(9,410)
Deferred revenues at end of period	$ 12,885	$ 22,367

During the years ended December 31, 2022 and 2021, the Company recognized revenue of $12.9 million and $9.4 million, respectively, related to deferred revenue that was recorded as a contract liability at the beginning of each respective year, respectively.

10. Patent License Agreement

On February 8, 2016, the Company entered into an exclusive patent license agreement with the Massachusetts Institute of Technology ("MIT") whereby MIT granted an exclusive royalty bearing license to the Company to develop, manufacture and commercialize products covered by certain patent rights owned by MIT The Company also has various rights to grant sublicenses.

Under the terms of the agreement, the Company paid an upfront license issuance fee of $0.1 million and is also obligated to pay annual maintenance fees to MIT, all of which are recognized as research and development expense in the statement of operations. All annual minimum payments are fully creditable against royalties subsequently due on net sales of licensed products earned in the same calendar year. The Company also must pay MIT a royalty percentage in the low single digits on all net sales of licensed products and a royalty percentage in the low to mid double digits on any sublicensing revenue. In addition, the Company is obligated to make aggregate milestone payments to MIT of up to $2.1 million upon achievement of specified milestones related to the initiation and execution of clinical trials and first commercial sale of a product.

The term of the license agreement will continue until the later of (i) the expiration of the last valid claim within the patent rights covering the product in such country, (ii) the consequence of certain patent challenges or (iii) default. Under terms of the agreement. MIT may terminate the agreement in the event (i) the Company fails to pay any amount due when required to be made and fails to cure such failure within thirty (30) days after receipt of notice from MIT, (ii) is in material breach of its diligence obligations under the agreement and fails to remedy within ninety (90) days after receipt of notice, (iii) is in any other material breach under the agreement and fails to remedy within sixty (60) days after receipt of notice, (iv) declares insolvency or bankruptcy or (v) the Company or a sublicensee brings a patent challenge. The Company may terminate the agreement at any time on written notice to MIT at least ninety (90) days prior to the termination date specified in the notice. Upon expiration or termination of the agreement, all rights revert to MIT.

11. Income Taxes

For the years ended December 31, 2022 and 2021, the Company recorded no income tax benefits for the net operating losses incurred or for the research and development tax credits generated in each period in U.S Federal and Massachusetts, due to its uncertainty of realizing a benefit from those items. All the Company's operating losses since inception have been generated in the United States.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2022	2021
Federal statutory income tax rate	21.0 %	21.0 %
State income taxes, net of federal benefit	6.0	6.3
Federal and state tax credits	7.3	6.3
Stock-based compensation	(1.0)	0.1
Other	(0.1)	—
Change in deferred tax asset valuation allowance	(33.2)	(33.7)
Effective income tax rate	0.0 %	0.0 %

Net deferred tax assets as of December 31, 2022 and 2021 consisted of the following (in thousands):

	Year Ended December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 53,823	$ 49,145
Research and development tax credit carryforwards	17,645	14,446
Lease liabilities	2,566	3,670
Deferred revenue	3,525	6,115
Accrued expense and other liabilities	1,066	585
Capitalized R&E expenses	7,688	—
Other	2,658	1,627
Total deferred tax assets	88,971	75,588
Less: Valuation Allowance	(86,276)	(71,818)
Total net deferred tax assets	2,695	3,770
Deferred tax liabilities:		
Lease right-of-use assets	(2,457)	(3,517)
Fixed assets	(238)	(253)
Total deferred tax liabilities	(2,695)	(3,770)
Net deferred tax assets	$ —	$ —

As of December 31, 2022, the Company had U.S. federal net operating loss carryforwards of $197.7 million, which may be available to offset future taxable income, of which $10.5 million of the total net operating loss carryforwards expire at various dates beginning in 2036, while the remaining $187.2 million do not expire but are limited in their usage to 80% of annual taxable income. In addition, as of December 31, 2022, the Company had state net operating loss carryforwards of $193.4 million, which may be available to offset future taxable income and expire at various dates beginning in 2037.

As of December 31, 2022, the Company also had federal and state research and development tax credit carryforwards of $9.2 million and $5.0 million, respectively, which may be available to reduce future tax liabilities and expire at various dates beginning in 2037 and 2032, respectively. In addition, the Company had Orphan Drug Designations granted by the Food and Drug Administration ("FDA") for SIG-001, SIG-005 and SIG-007, but withdrew their

designations for SIG-001 and SIG-005 during the year. The Company generated an orphan drug credit in the amount of $4.5 million which may be available to reduce future tax liabilities and begin to expire in 2039.

Utilization of the net operating loss and research and development credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, and corresponding provisions of state law, due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company completed a Section 382 study for the tax period from the Company's inception through December 31, 2019 and concluded that $0.4 million of net operating losses generated before February 10, 2016 is more likely than not subject to restrictive limitation and reduced the net operating loss carryforward balance. There could also be additional ownership changes in the future which may result in additional limitations on the utilization of net operating loss carryforwards and credits.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize its deferred tax assets, which are composed principally of net operating loss carryforwards. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of its federal and state net deferred tax assets. Accordingly, a full valuation allowance has been established against the net deferred tax assets as of December 31, 2022 and 2021. The Company reevaluates the positive and negative evidence at each reporting period.

The changes in the valuation allowance for deferred tax assets during the years ended December 31, 2022 and 2021 related primarily to the increases in net operating loss carryforwards, research and development tax credits generated and the deferred tax assets related to deferred revenue. The changes in the valuation allowance for 2022 and 2021 were as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Valuation allowance at beginning of year	$ 71,818	$ 45,735
Increases recorded to income tax provision	14,458	26,083
Valuation allowance at end of year	$ 86,276	$ 71,818

The Company assesses the uncertainty in its income tax positions to determine whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals of litigation processes, based on the technical merits of the position. For the tax position meeting the more-likely-than-not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than 50% likelihood of being realized upon the ultimate settlement with the relevant taxing authority. As of December 31, 2022 and 2021, the Company had not recorded any reserves for uncertain tax positions or related interest and penalties.

The Company files income tax returns as prescribed by the tax law of the jurisdiction in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdiction, where applicable. As of December 31, 2022 and 2021, there were no pending tax examinations. Since the Company is in a loss carryforward position, it is generally subject to examination by the U.S. federal, state, and local income tax authorities for all tax years in which a loss carryforward is available.

12. Commitments and Contingencies

401(k) Plan

In January 2017, and as amended in January 2019, the Company established a defined-contribution plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Starting in 2020, the Company makes matching contributions at a rate of 100% of each employee's contribution up

to a maximum employee contribution of 3% of eligible plan compensation. For each of the years ended December 31, 2022 and 2021, the Company made matching contributions of $0.3 million and $0.4 million, respectively.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and certain of its executive officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. The Company has not incurred any material costs as a result of such indemnifications and is not currently aware of any indemnification claims.

Legal Proceedings

The Company is not a party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses as incurred the costs related to such legal proceedings.

13. Leases

Corporate headquarters

In August 2017, the Company entered into an operating lease agreement for its corporate headquarters located at 100 Binney Street, Cambridge, Massachusetts. The term of the lease commenced in February 2018 and is scheduled to expire in February 2025. Under the terms of the lease, the Company provided a security deposit of $0.6 million, which is included in restricted cash in the accompanying balance sheets. The lease provides for annual rent escalations. The Company pays for its proportionate share of building operating costs such as maintenance, utilities, and insurance that are treated as variable costs and excluded from the measurement of the lease. The Company is entitled to one option to extend the lease term for an additional three years. The option to extend the lease term was not included in the right-of-use asset and lease liability as it was not reasonably certain of being exercised.

In October 2019, the Company entered into an assignment agreement in which it agreed to take over a lease of office and laboratory space adjacent to its current headquarters at 100 Binney Street in Cambridge, Massachusetts. The lease commenced on October 16, 2020, the date in which the space was delivered to the Company, and expires in February 2025. Under the terms of the lease, the Company provided a security deposit of $0.5 million, which is included in restricted cash in the accompanying balance sheets. The lease provides for annual rent escalations. The Company pays for its proportionate share of building operating costs such as maintenance, utilities, and insurance that are treated as variable costs and excluded from the measurement of the lease. The Company does not have an option to extend the lease term.

Manufacturing Services Agreement

In June 2019, the Company entered into a development and manufacturing services agreement for the commercial production of its Encapsulated Cell Product. The Company was required to pay an up-front suite reservation fee of $0.3 million and is required to pay a $0.1 million per month suite fee as well as certain labor, raw materials, testing and shipping costs for manufacturing services through September 2020, the initial term of the agreement. The Company concluded that this agreement contains an operating lease as the suite is designated for its exclusive use during the term of the agreement. Upon commencement in September 2019, the Company recorded a right-of-use asset of $1.7 million, inclusive of prepaid rent and a lease liability of $1.4 million. The Company recognizes lease expense on a straight-line basis over the term of the lease.

In March 2020, the Company elected to extend its use of the designated suite through June 30, 2021 resulting in the remeasurement of the operating lease. Accordingly, the operating lease liability and corresponding right-of-use asset were increased by $1.1 million. In March 2021 and September 2021, the Company elected to extend its use of the designated suite through December 31, 2021 and July 31, 2022, respectively. Accordingly, the operating lease liability and corresponding right-of-use asset were increased by a total of $1.4 million. In December 2021, the Company elected to terminate its use of the designated suite effective March 31, 2022. Accordingly, the operating lease liability and corresponding right-of-use assets were decreased by $0.5 million.

Finance leases

The Company does not have any material finance leases as of December 31, 2022 and 2021.

Summary of lease costs

The components of lease cost under ASC 842 were as follows (in thousands):

	Year Ended December 31,	
Lease costs	**2022**	**2021**
Operating lease cost	$ 4,827	6,029
Short term lease cost	679	679
Variable lease cost	724	1,101
Total lease cost	$ 6,230	$ 7,809

Supplemental disclosure of cash flow information related to leases was as follows (in thousands):

	Year Ended December 31,	
	2022	**2021**
Cash paid for amounts included in the measurement of operating lease liabilities (operating cash flows)	$ 4,844	$ 5,965
Lease assets obtained in exchange for new operating lease liabilities	$ 68	$ 917

The weighted-average remaining lease term and discount rate were as follows:

	Year Ended December 31,	
	2022	**2021**
Weighted-average remaining lease term (in years)	2.2 years	3.1 years
Weighted-average discount rate	8.4 %	8.4 %

The following table presents the maturity of the Company's operating lease liabilities as of December 31, 2022 (in thousands):

Year Ending December 31,	
2023	$ 4,599
2024	4,734
2025	802
2026	—
2027	—
Thereafter	—
Total future minimum lease payments	10,135
Less: imputed interest	(842)
Present value of operating lease liability	$ 9,293

14. Net Loss per Share

Net Loss per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2022	2021
Numerator:		
Net loss	$ (43,561)	$ (77,311)
Net loss attributable to common stockholders	$ (43,561)	$ (77,311)
Denominator:		
Weighted average common stock outstanding—basic and diluted	32,405,786	31,860,264
Net loss per share attributable to common stockholders—basic and diluted	$ (1.34)	$ (2.43)

The Company's potential dilutive securities have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2022	2021
Warrants to purchase common stock	19,044	19,044
Future issuable shares under the employee stock purchase plan	56,720	33,650
Unvested restricted stock units	150,400	275,400
Stock options to purchase common stock	4,912,386	3,138,646
	5,138,550	3,466,740

15. Related Party Transactions

The Company has a patent license agreement with MIT and issued 333,333 shares of its common stock to MIT as part of the consideration for this patent license (Note 10). Additionally, through the completion of the Company's IPO two members of the Company's board of directors were employed by MIT and subsequent to the IPO one member of the Company's board of directors is employed by MIT. The Company incurs charges for the use of certain MIT equipment and facilities. For the years ended December 31, 2022 and 2021, the Company incurred expenses of $0.4 million and $0.1 million, respectively, related to business with MIT. As of December 31, 2022 and 2021, there was less than $0.1 million and $0 recorded in accounts payable due to this related party.

As described in Note 9 above, the Company entered into the 2018 Lilly Agreement with Lilly, a shareholder of the Company, in April 2018. During the years ended December 31, 2022 and 2021, the Company recognized $12.9 million and $9.5 million, respectively, of related party revenue associated with the Lilly collaboration agreements. As of December 31, 2022 and 2021, the Company had deferred revenue related to the collaboration agreements with Lilly of $12.9 million and $22.4 million, respectively. As of December 31, 2022 and 2021, we had $2.2 million and $0.1 million in accounts receivable with Lilly, respectively. As of December 31, 2022 we had $1.3 million in unbilled accounts receivable with Lilly and as of December 31, 2021 we did not have unbilled accounts receivable.

On February 1, 2022, the Company entered into a shared space arrangement with a portfolio company of Flagship Pioneering, to sublease a portion of its office and laboratory space in Cambridge, Massachusetts. The term of the shared space arrangement commenced on February 1, 2022 and continues for an initial term ending on July 31, 2023. The agreement may be renewed for six successive one-month periods. The Company will be paid a fee based on the portfolio company's occupancy of the office and laboratory space. Under this agreement, the Company recorded other income, net,

of $0.2 million during the year ended December 31, 2022. The Company received $3.0 million of cash payments during the year ended December 31, 2022, and as of December 31, 2022, the Company had no outstanding receivables under this agreement.

In January 2021, the Company entered into a shared space arrangement with a portfolio company of Flagship Pioneering, one of the Company's significant stockholders, to sublease a portion of its office and laboratory space in Cambridge, Massachusetts. The term of the shared space arrangement commenced in January 2021 and ended on December 31, 2021. Under this agreement, the Company recorded other income of $0.4 million during the year ended December 31, 2021. The Company received cash payments of $0.4 million during the year ended December 31, 2021.

Item 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

Item 9A. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer (our principal executive officer and principal financial officer as of December 31, 2022), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022 and concluded that our disclosure controls and procedures were effective as of that date. The term "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, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Management's Report on Internal Control Over Financial Reporting

Management is responsible for establishing and maintaining adequate "internal control over financial reporting," as such term is defined under Rule 13a-15(f) of the Exchange Act. We maintain internal control over financial reporting designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles ("U.S. GAAP").

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

Management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2022. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control—Integrated Framework (2013). Based on this assessment, management has concluded that the Company's internal control over financial reporting was effective as of December 31, 2022. As a non-accelerated filer, we are not required to comply with the auditor attestation requirement of Section 404 of the Sarbanes-Oxley Act of 2002.

Changes in Internal Control over Financial Reporting

There were no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the quarter ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2022.

Item 11. EXECUTIVE COMPENSATION

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2022.

Item 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2022.

Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2022.

Item 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2022.

PART IV

Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) Documents filed as a part of this Report:

(1) Financial Statements—The financial statements listed in the Index to Financial Statements beginning on page 138 are filed as part of this Annual Report on Form 10-K.

(2) Financial Statement Schedules—There are no Financial Statement Schedules included with this filing for the reason that they are not applicable or are not required or the required information is included in the Financial Statements or Notes listed in the Index to Financial Statements beginning on page 134.

(b) Index to Exhibits

Exhibit number	Description of document
3.1	Fifth Amended and Restated Certificate of Incorporation of Sigilon Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on December 8, 2020 (File No. 333-250070))
3.2	Amended and Restated Bylaws of Sigilon Therapeutics, Inc. (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed with the SEC on December 8, 2020 (File No. 333-250070))
4.1	Specimen stock certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
4.2	Third Amended and Restated Investors' Rights Agreement, by and among Sigilon Therapeutics, Inc. and the investors party thereto, dated as of October 23, 2020 (incorporated by reference to Exhibit 4.2 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
4.3	Form of Warrant to Purchase Stock, between Sigilon Therapeutics, Inc. and Oxford Finance LLC, dated September 2, 2020 (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
4.4	Description of Registered Securities Pursuant to Section 12 of the Securities Exchange Act of 1934 (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form 10-K for the year ended December 31, 2021 (File No. 001-39746))
10.1	Lease, by and between ARE-MA Region No. 45, LLC and Sigilon Therapeutics, Inc., dated August 28, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.2	Lease Agreement, by and between ARE-MA Region No. 45, LLC and Foghorn Therapeutics Inc., dated August 24, 2017 (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.3	Assignment and Assumption of Lease, by and between Foghorn Therapeutics Inc. and Sigilon Therapeutics, Inc., dated October 21, 2019 (incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.4	Consent to Assignment and First Amendment to Lease, by and among ARE-MA Region No. 45, LLC, Foghorn Therapeutics Inc. and Sigilon Therapeutics, Inc., dated October 21, 2019 (incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 (File No. 333-250070))

10.5	Second Amendment to Lease, by and among ARE-MA Region No. 45, LLC and Sigilon Therapeutics, Inc., dated January 19, 2021 (incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form 10-K for the year ended December 31, 2021 (File No. 001-39746))
10.6	Loan and Security Agreement, by and among Oxford Finance LLC, the Lenders party thereto, and Sigilon Therapeutics, Inc., dated September 2, 2020 (incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.7++	Exclusive Patent License Agreement, by and between Massachusetts Institute of Technology and Sigilon Therapeutics, Inc., dated February 8, 2016 (incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.8++	First Amendment to Exclusive Patent License Agreement, by and between Massachusetts Institute of Technology and Sigilon Therapeutics, Inc., dated February 2, 2017 (incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.9++	Second Amendment to Exclusive Patent License Agreement, by and between Massachusetts Institute of Technology and Sigilon Therapeutics, Inc., dated August 9, 2018 (incorporated by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.10++	Third Amendment to Exclusive Patent License Agreement, by and between Massachusetts Institute of Technology and Sigilon Therapeutics, Inc., dated November 6, 2019 (incorporated by reference to Exhibit 10.9 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.11++	Fourth Amendment to Exclusive Patent License Agreement, by and between Massachusetts Institute of Technology and Sigilon Therapeutics, Inc., dated December 10, 2020 (incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form 10-K for the year ended December 31, 2021 (File No. 001-39746))
10.12++	Fifth Amendment to Exclusive Patent License Agreement, by and between Massachusetts Institute of Technology and Sigilon Therapeutics, Inc., dated September 17, 2021 (incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form 10-Q for the quarter ended September 30, 2021 (File No. 001-39746))
10.13++	Sixth Amendment to Exclusive Patent License Agreement, by and between Massachusetts Institute of Technology and Sigilon Therapeutics, Inc., dated February 1, 2022 (incorporated by reference to Exhibit 10.13 to the Company's Registration Statement on Form 10-K for the year ended December 31, 2021 (File No. 001-39746))
10.14++	Research Collaboration and Exclusive License Agreement, by and between Sigilon Therapeutics, Inc. and Eli Lilly and Company, dated April 2, 2018 (incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.15++	First Amendment to Research Collaboration and Exclusive License Agreement by, and between Sigilon Therapeutics, Inc. and Eli Lilly and Company, dated May 5, 2022 (incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form 10-Q for the quarter ended June 30, 2022 (File No. 001-39746))
10.16+	Sigilon Therapeutics, Inc. 2016 Stock Option and Grant Equity Incentive Plan, as amended (incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1 (File No. 333-250070))

10.17+	Form of Incentive Stock Option Agreement under the Sigilon Therapeutics, Inc. 2016 Equity Incentive Plan (incorporated by reference to Exhibit 10.12 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.18+	Form of Nonstatutory Stock Option Agreement under the Sigilon Therapeutics, Inc. 2016 Equity Incentive Plan (incorporated by reference to Exhibit 10.13 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.19+	Offer Letter, between Sigilon Therapeutics, Inc. and Rogerio Vivaldi Coelho, M.D., dated April 23, 2018 (incorporated by reference to Exhibit 10.14 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.20+	Severance Waiver and Offer Letter Amendment, between Sigilon Therapeutics, Inc. and Rogerio Vivaldi Coelho, M.D., dated October 26, 2020 (incorporated by reference to Exhibit 10.17 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.21+	Offer Letter, between Sigilon Therapeutics, Inc. and May Orfali, M.D. dated October 27, 2021 (incorporated by reference to Exhibit 10.24 to the Company's Registration Statement on Form 10-K for the year ended December 31, 2021 (File No. 001-39746))
10.22+	Consulting Agreement, dated October 13, 2021, between the Company and May Orfali, M.D. (incorporated by reference to Exhibit 10.28 to the Company's Registration Statement on Form 10-K for the year ended December 31, 2021 (File No. 001-39746))
10.23+*	Consulting Agreement, dated February 14, 2023, between the Company and May Orfali, M.D.
10.24+*	Letter Agreement, dated February 10, 2023, between the Company and May Orfali, M.D.
10.25+	Offer Letter, between Sigilon Therapeutics, Inc. and Philip Ashton-Rickardt, dated May 25, 2021 (incorporated by reference to Exhibit 10.25 to the Company's Registration Statement on Form 10-K for the year ended December 31, 2021 (File No. 001-39746))
10.26+*	Offer Letter, between Sigilon Therapeutics, Inc. and Sarah Yuan, dated January 12, 2022
10.27+*	Offer Letter, between Sigilon Therapeutics, Inc. and Josias Pontes, dated October 23, 2019
10.28+	Form of Non-Chief Executive Officer Severance Waiver and Offer Letter Amendment (incorporated by reference to Exhibit 10.18 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.29+	Sigilon Therapeutics, Inc. Amended and Restated Severance and Change in Control Policy (incorporated by reference to Exhibit 10.21 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.30+	Sigilon Therapeutics, Inc. 2020 Cash Incentive Plan (incorporated by reference to Exhibit 10.22 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.31+	Sigilon Therapeutics, Inc. Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.23 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.32+	Sigilon Therapeutics, Inc. 2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.24 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.33+	Form of Non-Statutory Stock Option Agreement under the Sigilon Therapeutics, Inc. 2020 Equity Incentive Plan (Non-Employee Directors) (incorporated by reference to Exhibit 10.25 to the Company's Registration Statement on Form S-1 (File No. 333-250070))

10.34+	Form of Non-Statutory Stock Option Agreement under the Sigilon Therapeutics, Inc. 2020 Equity Incentive Plan (Employees) (incorporated by reference to Exhibit 10.26 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.35+	Form of Incentive Stock Option Agreement under the Sigilon Therapeutics, Inc. 2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.27 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
10.36+*	Form of Restricted Stock Unit Agreement under the Sigilon Therapeutics, Inc. 2020 Equity Incentive Plan
10.37+	Sigilon Therapeutics, Inc. 2020 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.28 to the Company's Registration Statement on Form S-1 (File No. 333-250070))
21.1*	Subsidiaries of the Registrant
23.1*	Consent of PricewaterhouseCoopers LLP, an independent registered public accounting firm
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted 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
101.INS*	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document)
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101.*)

* Filed herewith

\+ Indicates management contract or compensatory plan

++ Portions of this exhibit (indicated by asterisks) have been redacted because they are both not material and the registrant customarily and actually treats such information as private or confidential.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

SIGILON THERAPEUTICS, INC.
By: /s/ Rogerio Vivaldi Coelho, M.D.
Rogerio Vivaldi Coelho, M.D.
President and Chief Executive Officer
(Principal executive officer)
Date: March 14, 2023

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Rogerio Vivaldi Coelho, M.D. Rogerio Vivaldi Coelho, M.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 14, 2023
/s/ Josias Pontes Josias Pontes	Senior Vice President, Chief Financial Officer (Principal Accounting and Principal Financial Officer)	March 14, 2023
/s/ Doug Cole, M.D. Doug Cole, M.D.	Chairman of the Board of Directors	March 14, 2023
/s/ John Cox John Cox	Director	March 14, 2023
/s/ Stephen Oesterle, M.D. Stephen Oesterle, M.D.	Director	March 14, 2023
/s/ Kavita Patel, M.D. Kavita Patel, M.D.	Director	March 14, 2023
/s/ Robert Ruffolo, Jr., Ph.D. Robert Ruffolo, Jr., Ph.D.	Director	March 14, 2023
/s/ Eric Shaff Eric Shaff	Director	March 14, 2023