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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2022

OR

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

FOR THE TRANSITION PERIOD FROM TO

Commission File Number 001-38663

Gritstone bio, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**47-4859534**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
5959 Horton Street, Suite 300	
Emeryville, CA	**94608**
(Address of principal executive offices)	**(Zip Code)**

(510) 871-6100

Registrant's telephone number, including area code

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**GRTS**	**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 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 assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

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

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

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the common stock held by non-affiliates of the registrant as of June 30, 2022 (the last business day of the registrant's most recently completed second fiscal quarter) was approximately $171.7 million, based on the closing price of the registrant's common stock, as reported by the Nasdaq Global Select Market on June 30, 2022 of $2.42 per share. Shares of the registrant's common stock held by each executive officer, director, and holder of 5% or more of the outstanding common stock have been excluded in that such persons may deemed to be affiliates. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

The number of shares of Registrant's Common Stock outstanding as of March 7, 2023 was 87,661,978.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement relating to the Annual Meeting of Shareholders, scheduled to be held on June 16, 2023, are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such Definitive Proxy Statement will be filed with the Securities and Exchange Commission within 120 days after the fiscal year to which this report relates.

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PART I

Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K, including "Business" in Part I Item I and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II Item 7, contains "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (Exchange Act). All statements other than statements of historical fact are statements that could be deemed forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "potential," "positioned," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the sufficiency of our capital resources and timing of our cash runway, as well as our actual needs for additional financing and our ability to obtain additional capital;
- our clinical and regulatory development plans for our product candidates;
- our expectations regarding the potential market size and size of the potential patient populations for our product candidates, in particular those within the GRANITE®, SLATE® and CORAL programs, and any future product candidates with limited patient populations, if approved for commercial use;
- our expectations regarding the data to be derived in our ongoing and planned clinical trials including, in particular, our expectations for the size and design of our planned clinical trials, timing of commencement and initiation of our trials and the timing of the availability of data from such trials;
- our expectations regarding our Gritstone EDGE™ artificial intelligence and vaccine platforms, including our ability to utilize (i) our Gritstone EDGE™ platform to predict the tumor-specific neoantigens that will be presented on a patient's tumor cells and identify highly conserved T cell epitopes for durable protection for infectious diseases and (ii) our vaccine platform to deliver selected antigens to the patient's immune system to drive the destruction of tumors or virally-infected cells;
- the timing of commencement of our future nonclinical studies, clinical trials and research and development programs;
- our ability to discover, develop and advance product candidates into, and successfully complete, clinical trials;
- our plans and strategy regarding maintaining existing and entering into new collaborations and/or partnerships;
- the timing or likelihood of regulatory filings and approvals for our product candidates;
- our expectations with respect to the commercialization, marketing and manufacturing of our product candidates;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model and strategic plans for our business, product candidates and technology platforms, including additional indications for which we may pursue;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates, including the projected terms of patent protection;
- our expectations regarding the impact of the COVID-19 pandemic or the end of the COVID-19 pandemic on our operations;
- the accuracy of our estimates of our expenses, future revenue and capital requirements;
- our future financial performance; and
- developments and projections relating to our competitors and our industry, including competing therapies.

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under "*Item 1A. Risk Factors*" and elsewhere in this Annual Report on Form 10-K. Any forward-looking statement in this Annual Report on Form 10-K reflects our current views with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Given these uncertainties, you should not place undue reliance on these forward-looking

statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates, including data regarding the estimated patient population and market size for our product candidates, as well as data regarding market research, estimates and forecasts prepared by our management. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data are derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph are derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

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

Note Regarding Company References

Unless the context otherwise requires, the terms "Gritstone," "the Company," "we," "us," and "our" in this Annual Report on Form 10-K refer to Gritstone bio, Inc. and its subsidiary.

Item 1. Business.

Overview and Strategy

We are a clinical-stage biotechnology company focused on combining immunological insights with proprietary technologies and capabilities to develop next-generation vaccines. Specifically, we discover, develop, manufacture and deliver vaccine-based immunotherapy candidates against cancer and infectious disease. Our goal is to unlock more potent and durable immunity by harnessing vaccine innovation. We aim to achieve that goal by leveraging our in-house capabilities and technologies to address the shortcomings of currently available vaccines and immunotherapies.

The immune system sits at the nexus of many diseases and we believe that immune response modulation is core to several transformational product classes. Recent advances have pointed to T cells as being central to the success of cancer immunotherapy and critical in the elimination of virally infected cells. We believe that our scientific approach of focusing on generating antigen-specific T cells, particularly the challenging but critical cytotoxic CD8+ T cell subclass has the potential to drive transformational therapeutic and prophylactic benefits.

In oncology, we develop personalized vaccines that aim to destroy tumors through CD8+ (killer) T cell recognition of tumor cells by virtue of their surface display of neoantigens, peptides that are presented on cancer cells when certain mutations occur in tumor DNA. We have two clinical-stage oncology programs, both for common solid cancers. The first, GRANITE, focuses on development of individualized vaccines based on each patient's tumor DNA/RNA sequence (i.e., each vaccine is developed for each individual patient). The second, SLATE, focuses on development of "off-the-shelf" vaccines for sets of patients that share common tumor antigens including neoantigens. The scientific approaches to GRANITE and SLATE are similar, and we believe the technologies we developed to execute against them, i.e., to identify neoantigens accurately and deploy powerful killer T cell-stimulating vectors to deliver them, are capable of driving more potent and durable immune responses. In infectious disease, we develop both therapeutic and prophylactic vaccines targeting both T cells and B cells. We believe we are leading the field of development and application of self-amplifying mRNA (samRNA), a rapidly-emerging platform technology. Our unique approach to immunogen design, whereby our vaccines deliver, as appropriate, whole proteins to drive neutralizing antibodies (nAbs) and/or protein fragments to drive T cell responses, has the potential to both neutralize incoming pathogens (through nAbs) and kill infected cells through CD8+ T cell recognition of foreign, pathogen-derived peptides displayed on the surface of infected cells.

Our Key Technologies and Capabilities

Epitope Discovery: Gritstone EDGE™ (Epitope Discovery for GEnomes) Antigen Discovery and T cell Target Identification Platform

Antigen presentation to T cells is hard to predict since multiple biological steps must be comprehended within any prediction system, and antigenic peptide fragments are displayed on the cell surface by highly variable human leukocyte antigen (HLA) molecules that vary subject-to-subject. Our proprietary epitope discovery platform, EDGE™, has demonstrated the ability to offer accurate identification of T cell antigens that can be recognized by the immune system on tumor or virally-infected cells.

In the case of tumor cells, mutations in tumor DNA provide a large set of altered candidate protein fragments that the immune system can recognize. In cancer, we use EDGE™ to identify and select those mutations that are most likely to serve as tumor-specific neoantigens (TSNA), i.e., those neoantigens on the tumor that will best serve as targets for killer T cells.

Developing cancer immunotherapies that include tumor-specific neoantigens is challenging because tumors typically have hundreds of mutations, but only a small percentage of such mutations result in tumor-specific neoantigens (TSNA). Using EDGE™, we are able to sequence data from a patient's routine core needle tumor biopsy in an effort to predict which mutations will generate TSNAs most likely to be presented on the tumor cell surface by the patient's particular human leukocyte antigens (HLA).

We believe that EDGE™ leads the field in TSNA identification and previously available technologies are not able to predict the presence of TSNA with sufficient accuracy to design an effective therapy. We have observed a 9-to10-fold improvement in prediction performance with our EDGE™ platform compared to traditional approaches and published these data in Nature Biotechnology in December 2018. We continue to improve on EDGE and intend to continue optimizing its use for our cancer and infectious disease applications.

In infectious disease, we use EDGE™ to analyze the DNA/RNA sequence of a pathogen with the goal of predicting which gene fragments will likely function as T cell antigens on the surface of virally-infected cells. EDGE™ allows us to design the components of our vaccine candidates to include the specific target antigens for administration to humans (immunogens), with the aim of generating

strong immune responses to those antigens to achieve a desired biological effect. Such immune responses can be prophylactic (e.g., protecting against viral infections) or therapeutic (e.g., treating virally infected individuals with the aim to eradicate the virus).

The first US patent covering the EDGE™ technology was issued to us in 2018. We are working to identify novel classes of tumor antigens and continually improve the performance of EDGE™.

Next-generation Proprietary Vectors (ChAd and samRNA)

Following the identification of suitable targets with the help of EDGE™, we encode such targets within our vaccine vectors to deliver the payload and stimulate the immune system. We have developed two proprietary vectors that we deploy with the aim of eliciting the desired immune response; chimpanzee adenovirus (ChAd) and self-amplifying mRNA (samRNA). ChAd is well-recognized as a leading vector for induction of CD8+ (killer) T cells. samRNA is a next-generation RNA platform technology that has the potential to offer benefits over mRNA relevant to oncology and infectious disease. We selected ChAd and samRNA because we believe they are the best vectors for inducing and boosting CD8+ T cells in our personalized cancer vaccine programs. We believe our proprietary ChAd and samRNA vectors lead the field.

In oncology, we deploy both vectors via a heterologous prime-boost (vaccination with one vector followed by the other, in this case ChAd then samRNA). In infectious disease, we deploy one or both vectors based on the desired therapeutic or prophylactic immune response. The independent and "mix and match" application of our vectors is one of Gritstone's core competencies.

Chimpanzee Adenovirus 68 (ChAd)

ChAd vectors have been utilized in clinical studies in infectious disease and oncology over the past 20 years. They have been demonstrated to be well tolerated and effective at generating rapid and substantial CD8+ and CD4+ T cell responses. Additionally, ChAd vectors can induce B cell immune responses, i.e., elicit nAbs. We have developed a proprietary ChAd vector employing an E4 deletion to improve viral production efficiency in manufacturing.

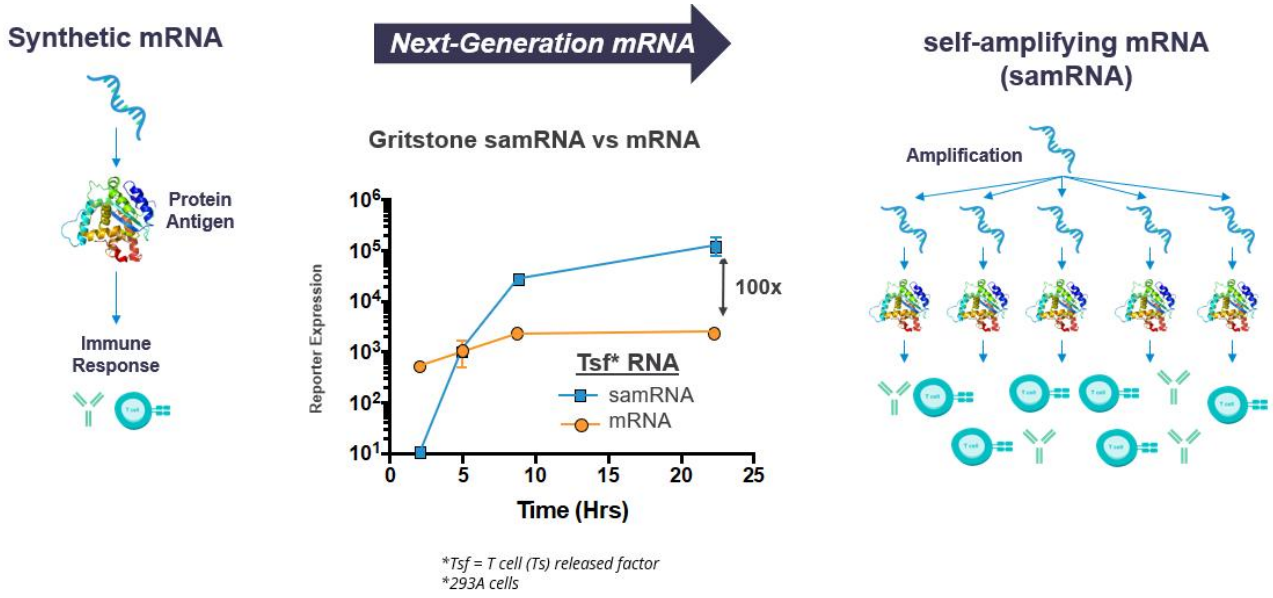
self-amplifying mRNA (samRNA)

Gritstone was the first to introduce samRNA encapsulated in lipid nanoparticles (LNP) into clinical trials in 2018. We believe that samRNA has the ability to boost pre-existing T cell responses and the potential to drive differentiated immune responses (potent and durable) in infectious disease.

Our samRNA vector is based on a synthetic RNA molecule derived from a wild-type Venezuelan Equine Encephalitis Virus (VEEV) replicon with the goal of extending the duration and magnitude of immunogen expression to drive potent and durable immune responses. Our samRNA is delivered in a LNP formulation. We are deploying this vector across our clinical stage programs. Like traditional mRNA vaccines, samRNA vaccines use the host cell's transcription system to produce target antigens to stimulate adaptive immunity. Unlike traditional mRNA, the RNA replicates once inside the cell, theoretically leading to high and durable antigen expression.

Potential benefits of samRNA may include extended duration and magnitude of antigen expression, strong and durable induction or boosting of neutralizing antibody and T cell immunity (CD8+ and CD4+), dose sparing, and a refrigerator-stable product.

Figure 1. Self-amplifying mRNA (samRNA) replicates within transduced cells, potentially driving stronger and more durable immune responses compared to traditional mRNA vaccines



In-house GMP Manufacturing

We manufacture our products at our own fully-integrated good manufacturing practice (GMP) biomanufacturing facilities. Our ability to control the manufacturing of high-quality vaccine products, and scale production, if early data are positive, is critical for efficient clinical development and commercialization. We have invested significant resources in our Cambridge, Massachusetts sequencing lab and our Pleasanton, California biomanufacturing facility to address these needs and position ourselves to control the critical steps in the production of our immunotherapy candidates.

Immunogen Design

Immunogen design is a key element in vaccine development, and a foundational aspect of design is understanding how vaccines might work for each individual application. Understanding how to elicit specific beneficial T cell responses is crucial to the development of effective therapeutic cancer vaccines. Successful vaccine strategies for infectious disease pathogens require wholly different approaches for the elicitation of antibodies to the pathogen surface antigen.

Our unique approach to immunogen design, whereby our vaccines can deliver both surface antigens to drive neutralizing antibodies (nAbs) and protein fragments to drive T cell responses, enables us to optimize our vaccine candidates to engage both arms of the immune system for both antibody and T cell production. Due in part to our chimeric design capabilities, our vaccines have the potential to both neutralize incoming pathogens (through nAbs) and kill infected cells through CD8+ T cell recognition of foreign, pathogen-derived peptides displayed on the surface of infected cells.

Translational Immunology

Through our work, we gain invaluable insights that go from “bench-to-manufacturing-to-bedside” and back at Gritstone. We have processes in place to translate these insights across our internal functions and systems to optimize our vaccine innovation efforts, incorporate them into our research and development work, advance our programs and optimize our product candidates throughout the development cycle.

A notable example of our translational work is within SLATE, our program focused on developing an “off the shelf” neoantigen immunotherapy for oncology, where we utilized outcomes from our first candidate (SLATE v1) to develop an optimized, second

candidate (SLATE-KRAS), which has since exhibited immunogenic superiority over SLATE v1 in both model systems and in humans. Our continuous learnings regarding fundamental mechanisms of innate and adaptive immunity, including the interplay between CD4+ and CD8+ T cell development, and the evolution of antibody responses following vaccination, are a key element in our effort to develop potent and durable vaccines.

Our Strategy

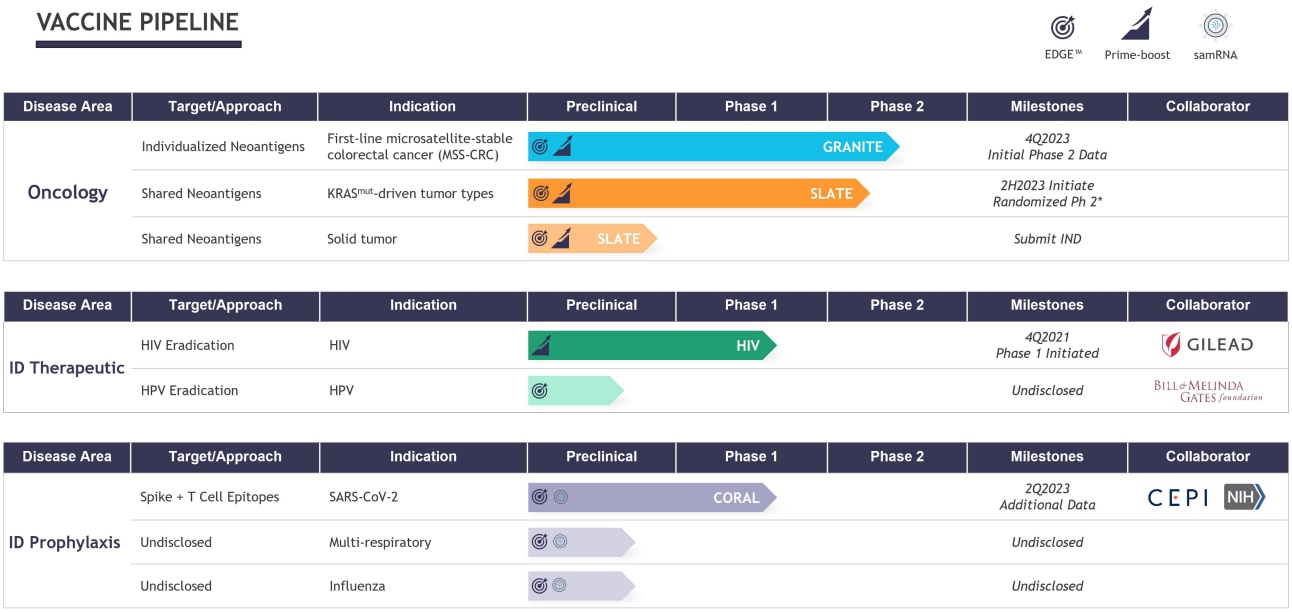
We believe that our team of industry leaders, each possessing specific expertise across our core disciplines of cancer genomics, immunology and vaccinology, clinical development, regulatory, and biomanufacturing, can successfully deliver groundbreaking vaccine-based immunotherapies for cancer and infectious disease by executing on the following strategic priorities:

- ***Continue leveraging our proprietary Gritstone EDGE™ platform and maximize its utility across modalities***. We use EDGE™ to predict, with high accuracy, tumor targets for our oncology programs. This is critical for our GRANITE program, where each patient's targets are individualized. We continue to improve EDGE by expanding its ability to identify novel classes of tumor antigens (such as gene fusions and alternative splicing) across our programs. We also use EDGE to predict viral epitopes for inclusion in our vaccine candidates against viral targets.
- ***Continue deploying and optimizing our next-generation vectors to drive potent and durable immune responses suited to the clinical context.*** Chimpanzee Adenovirus 68 (ChAd) and self-amplifying mRNA (samRNA) are our two vectors of choice based on their unique and synergistic properties. In multiple studies across our oncology and infectious disease platforms, we have exhibited the ability to deploy them individually and in combination to drive potent and durable immune responses based on the clinical context. We continue to improve and optimize these proprietary vectors for their use across our programs.
- ***Continue building, automating, and optimizing our in-house biomanufacturing capabilities to increase scalability and capacity.*** We believe the speed, quality, reliability, and scalability of our manufacturing capabilities is a core competitive advantage to our clinical development and potential commercial success. We have successfully internalized all biomanufacturing steps to drive down both cost and production time, as well as establish full control over intellectual property and product quality. We have internalized the majority of our quality control testing elements as well, though we outsource where prudent and feasible. We believe that operating our own manufacturing facility provides us with enhanced control of material supply for both clinical trials and the commercial market, will enable the more rapid implementation of process changes, and will allow for better long-term manufacturing cost control. We have the capability to manufacture every element involved in clinical development of our oncology vaccine-based immunotherapies.
- ***Continue advancing the GRANITE program through randomized, controlled trials with the goal of evaluating earlier lines of treatment and additional tumor types.*** Phase 1/2 clinical data to date have demonstrated initial positive safety results, induction of substantial neoantigen-specific CD8+ T cell responses and molecular responses for our individualized vaccine program. We are pleased with results observed with GRANITE to date in hard-to-treat, late-line CRC patients, and are optimistic we could see similar or better results from neoantigen immunotherapy in earlier lines of treatment where immune responses have the potential to be stronger and tumor genomic complexity is lower. GRANITE is now in a randomized Phase 2/3 clinical trial (GRANITE-CRC-1L) as a first-line maintenance treatment for microsatellite stable colorectal cancer (MSS-CRC). Within this study, we are also evaluating the potential of ctDNA as a new biomarker by which cancer progression could be measured. We believe the potential regulatory approval of our individualized vaccine candidate represents a potentially transformative development within cancer care.
- ***Continue advancing and optimizing our SLATE program to include other antigen classes to both broaden applicable patient population and drive multiple antigens per patient***. SLATE is our "off-the-shelf" TSNA-directed immunotherapy program for solid tumor cancers. SLATE vaccines are produced and delivered to clinical sites proactively, and can be administered rapidly upon patient selection (achieved by standard commercial screening for driver mutations). Phase 1/2 studies within SLATE have provided proof-of-concept for the approach and enabled optimization of the cassette based on results to date. We now believe the SLATE is now ready for "plug and play" application across solid tumor indications and shared tumor neoantigen classes. Our long-term vision is to continue optimizing this immunotherapy candidate to include other antigen classes to both broaden addressable patient population and also drive multiple antigens per patient.
- ***Conduct research and development on additional pathogens/infectious diseases.*** Our research pipeline focuses on the development of novel therapeutic and prophylactic vaccines across oncology and infectious diseases. Preclinical projects include a therapeutic HPV vaccine with support from the Bill and Melinda Gates Foundation, an influenza (flu) vaccine utilizing the samRNA vaccine platform and our capability of generating chimeric vaccine cassettes to drive broad and potent neutralizing antibodies and CD8+ T cells against these viruses, and a new combination respiratory vaccine candidate against multiple respiratory viruses.

Pipeline

Our unique capabilities have enabled us to advance potentially differentiated clinical assets across multiple therapeutic areas. The table below summarizes key information about our pipeline.

Figure 2. Our Pipeline



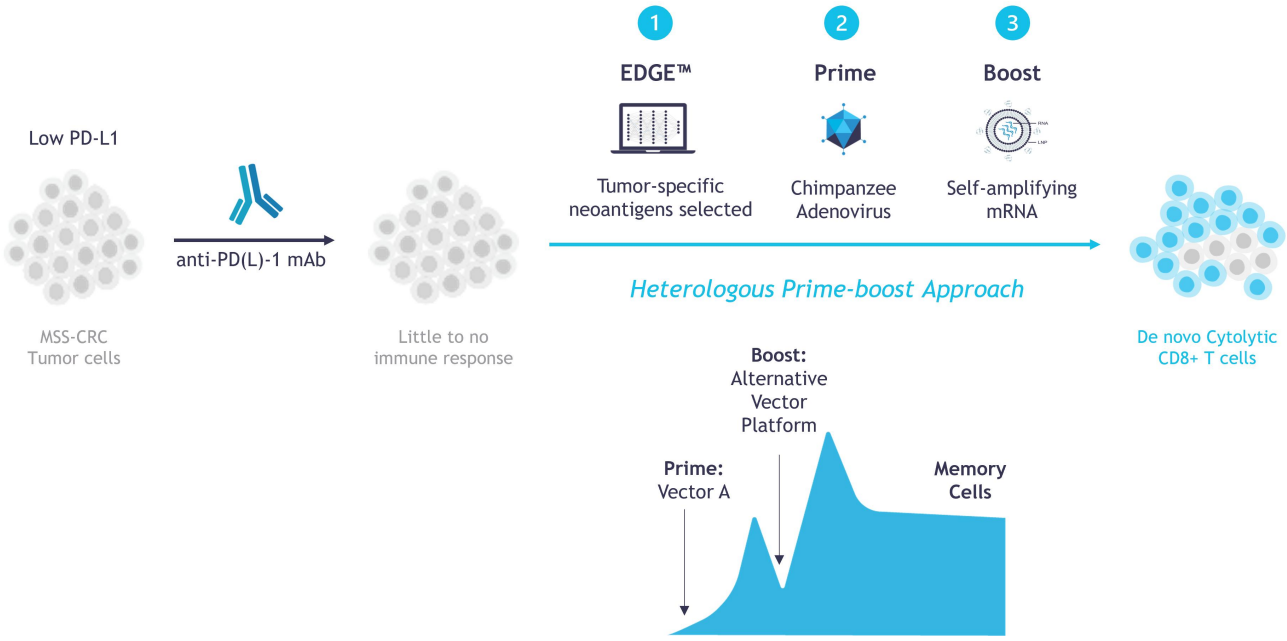
* Randomized trial in newly-diagnosed metastatic patients

Oncology Programs

Immuno-oncology (I-O) represents one of the most significant advances in the history of cancer treatment and has saved and extended the lives of an incalculable number of people since the discovery of the T cell receptor in 1982. However, despite the fields' advances, the benefits of today's immunotherapies, namely checkpoint inhibitors (CPIs), are limited only to those patients whose immune systems have recognized their tumor. Within CPI therapy, solid tumor patients, whose tumors have been infiltrated by CD8+ T cells (commonly referred to as "hot" tumors), typically respond to therapy, while the majority of patients, whose tumors lack immune infiltration (commonly referred to as "cold" tumors), typically develop disease progression and death. The primary challenge to the field today, and our approach to oncology, is to extend the positive outcomes seen in "hot" tumors to "cold" tumors by activating (aka "priming") de-novo aka naïve T cells, thus enabling the immune system to recognize the tumor and form an army of neoantigen-specific CD8+ T cells to enable tumor destruction.

Immunologically "cold" tumors represent many of the deadliest and 'hardest-to-treat' cancers we know today, and unleashing the immune system (notably CD8+ T cells) against them could represent the next transformational advance in I-O.

Figure 3. Gritstone's Approach: Induce CD8+ T cells Against "Cold" Solid Tumors Using Antigen Selection + Prime-boost Approach



Neoantigens are a novel class of targets for cancer immunotherapy and have been validated in cancer patients as potentially the most critical T cell targets. Neoantigens comprise short, tumor-specific, mutated peptide sequences presented on cancer cells, referred to as tumor-specific neoantigens (TSNA).

When a solid tumor patient responds to CPI therapy, there is abundant evidence they do so because T cells that recognize tumor-specific neoantigen (TSNA) are activated, enabling them to traffic to and engage the tumor. In GRANITE, we sequence the patients' tumor in-house and then use EDGE™ to identify those mutations most likely to serve as TSNA. In SLATE, identifying patients' driver mutations (and thus whether they are eligible for the "off the shelf" vaccine) can be done locally using commercially available sequencing.

The Prime-Boost Approach: Our Construct and Antigen Delivery System for GRANITE and SLATE

Having identified the proper neoantigens to incorporate the vaccine, the next step is to deliver the payload such that it primes naïve CD8+ T cells (activating and expanding them) and sustains their activity over time. To achieve this, we deploy a "heterologous prime-boost" immunization whereby we use ChAd to prime naïve T cells and samRNA to augment/sustain or "boost" the immune response (Figure 3 above). There is abundant literature demonstrating that the heterologous prime boost approach (whereby you "prime" with one vector and then "boost" with a different vector, both delivering the same antigens) can elicit greater and longer-lasting levels of immunity compared to the immune response obtained by single vaccination or by inoculations with the same vector.

Human infectious disease vaccine experience has taught us that the adenoviral vector is the vector of choice for priming a substantial T cell response consisting of cytotoxic CD8+ T cells (and, to a lesser degree, CD4+ T-helper cells). samRNA was selected as a likely vector of choice for boosting pre-existing T cells.

We believe that continued strong immune pressure upon the tumor is likely necessary to prevent immune escape by the tumor and drive a durable clinical response.

Our personalized vaccine candidates consist of (1) a prime vector and (2) a boost vector, both of which contain (3) a neoantigen cassette:

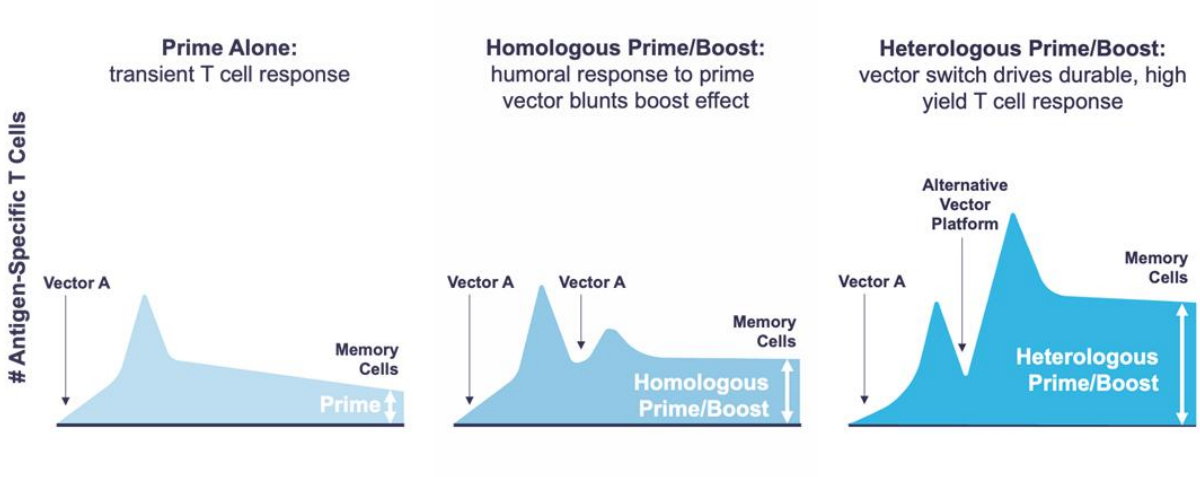
1. *Prime Vector (ChAd).* Our prime vector is a chimpanzee adenovirus (ChAd). We believe an adenoviral vector is one of the most potent antigen-delivery platforms to prime naïve T cells. There is extensive clinical experience demonstrating that

ChAd vectors are generally well tolerated and consistently generate rapid and substantial CD4+ and CD8+ T cell responses. Findings from our studies are consistent with these general observations.

2. *Boost Vector (samRNA).* Our boost vector is a self-amplifying mRNA (samRNA). Once in the cell, the injected source RNA replicates, amplifying the number of copies within the cells and leading to production of large amounts of the delivered target antigens. The presence of large quantities of antigen in an immune-stimulating environment drive profound antigen-specific T cell responses (adaptive immune responses). Additionally, samRNA has demonstrated the ability to be administered multiple times as a boost (aka safe and efficacious when 'repeat boosting'). Additional potential benefits of samRNA include extended antigen expression, nAb and T cell induction, and dose sparing potential.

3. *Neoantigen Cassette*. Within each of the two vectors used for the prime and boost immunizations, we include a cassette that contains neoantigens. For GRANITE, we have designed the cassette to contain 20 TSNA, based on several considerations, including TSNA prediction performance, breadth of the tumor-specific immune response and potential immune competition and manufacturing factors. The cassette is designed and made uniquely for each patient based upon their tumor sequence data and EDGE™-based TSNA predictions. For SLATE, the cassette is fixed for all patients, and contains common driver mutations (e.g. KRAS), which are known to be processed and presented by certain HLA molecules such as neoantigens that are shared between some patients. Most SLATE patients' tumors will only present a single neoantigen contained within the shared cassette. In contrast, although all of the mutations in a GRANITE cassette are contained within the patient's own tumor and can activate T cell responses post immunizations, it is expected that some of the delivered mutations, while present in the tumor genome, will not be processed and presented as a tumor cell surface neoantigenic HLA-peptide complex. We expect this to be acceptable, since these sequences are not wild-type (found in normal cells) and, therefore, only an irrelevant mutated peptide-specific immune response is expected to be elicited.

Figure 4. Comparison of Heterologous Prime-Boost with Homologous Prime-Boost and Prime Alone



Methods for evaluating efficacy, including circulating tumor DNA (ctDNA)

The standard method of evaluating early efficacy outcomes in advanced cancer therapy (radiology) is increasingly imprecise in immuno-oncology since it relies upon radiologic assessment of tumor size, with the assumption that tumor shrinkage is necessary for clinical benefit to ensue (RECIST criteria). We aim to drive T cells into lesions, wherein they proliferate and could temporarily increase tumor lesion size (radiologic pseudoprogression), rendering traditional radiologic tools uninformative and, possibly, misleading.

We believe that circulating tumor DNA (ctDNA) response data, together with overall survival figures, are the most appropriate and accurate methods to predict and measure outcomes from novel therapeutics such as ours, in patients with advanced, metastatic cancer. Data from Phase 1/2 studies of both GRANITE and SLATE have demonstrated an association between molecular response and overall survival, together with evidence of radiologic pseudoprogression at early timepoints.

GRANITE individualized neoantigen-based vaccine program

GRANITE is our individualized neoantigen-based vaccine program for solid cancers. Development of our GRANITE vaccines begins with receipt of a routine tumor biopsy from the patient. Next, we sequence the tumor sample in-house to identify tumor mutations and apply our proprietary EDGE™ platform to identify which mutations form TSNA most likely to be presented on the patient's tumor.

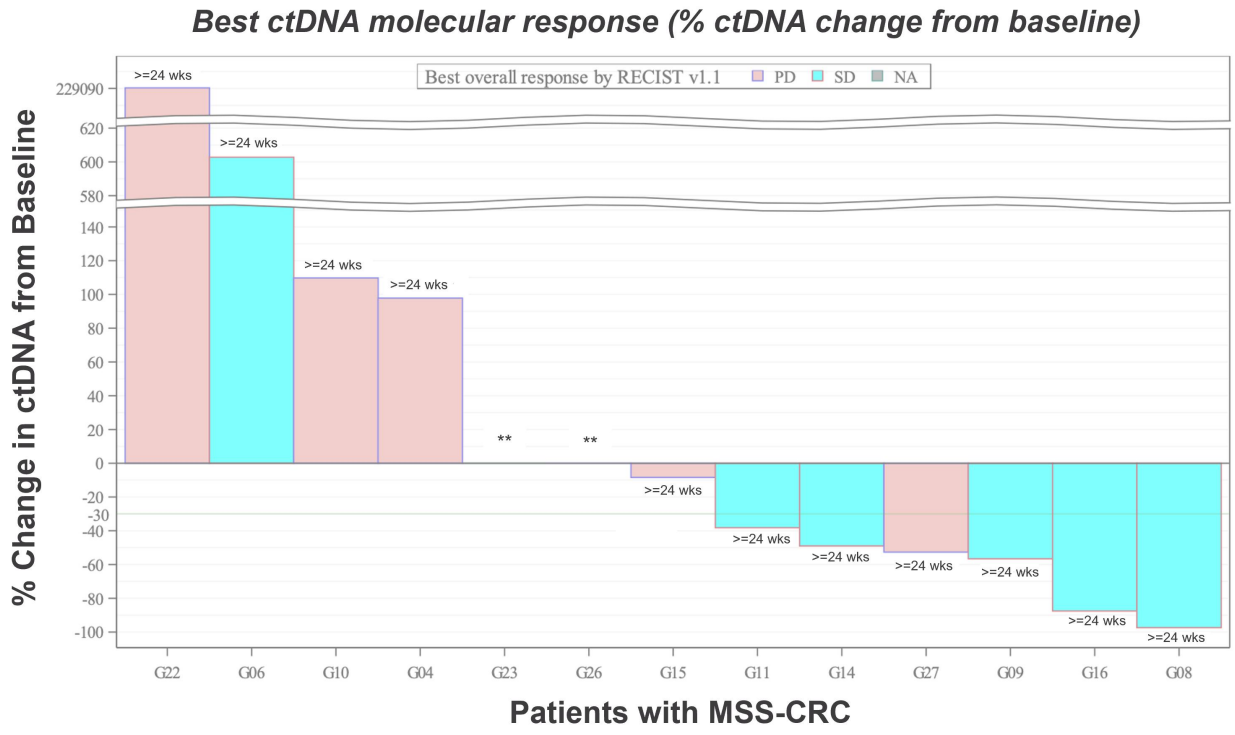
Using these TSNA, we design and manufacture a vaccine that contains the relevant neoantigens for that specific patient, which is administered by simple intramuscular injection alongside a patients' normal course of treatment. Our individualized immunotherapy candidates are designed to fit easily into a community oncology setting, where most oncology patients are treated. GRANITE was granted Fast Track designation by the Food and Drug Administration (FDA) for the treatment of microsatellite stable colorectal cancer (MSS-CRC).

Results from our ongoing Phase 1/2 study evaluating GRANITE combination with checkpoint inhibitors in 3rd line microsatellite-stable colorectal cancer (MSS-CRC) and other advanced solid tumors have demonstrated positive results. Among all cohorts, the vaccine regimen was shown to be generally well-tolerated with no dose limiting toxicities and demonstrated consistent and potent CD8+ neoantigen-specific T cell induction. Additionally, an association between molecular responses (as measured by reduction in circulating tumor DNA, ctDNA) and improved clinical outcomes (including overall survival) was observed in MSS-CRC subjects.

As of August 31, 2022, the median overall survival (mOS) among molecular responders in this cohort was 22 months (median not yet reached) and demonstrated a molecular response rate of 55% molecular (6/11 evaluable patients; molecular response defined as ≥30% reduction in ctDNA from baseline). This compares to mOS of 7.8 months in evaluable MSS-CRC patients who did not exhibit a molecular response in the study, and a general 6-7 months against standard of care (Trifluridine/tipiracil combo and Regorafenib monotherapy). Interim results from the Phase 1/2 study of GRANITE were published in Nature Medicine in August 2022.

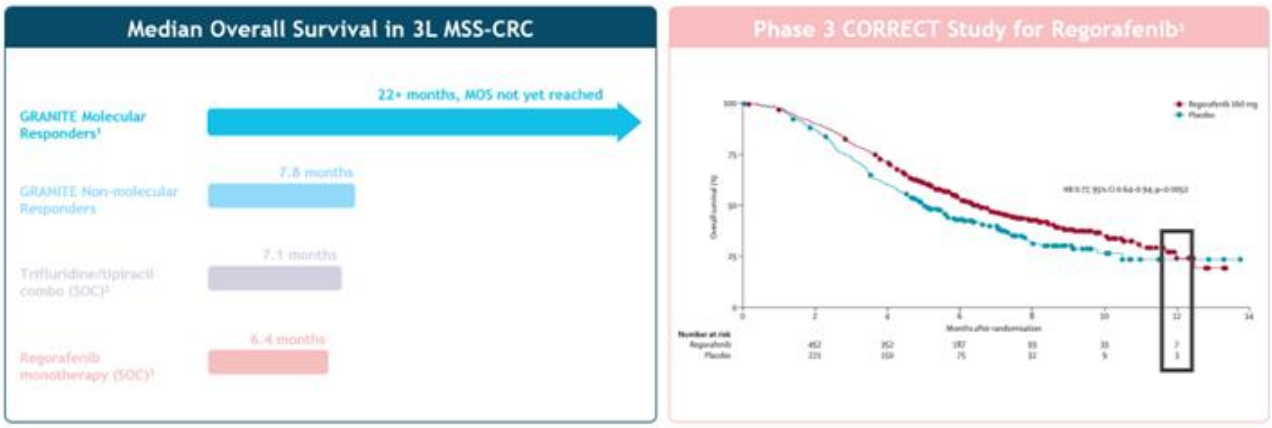
Upon assessing initial results of the GRANITE Phase 1/2 study, we discussed potential registrational paths with the FDA and subsequently initiated a randomized, controlled Phase 2/3 trial in newly diagnosed metastatic CRC patients that has registrational intent (NCT05141721). The study, which is evaluating GRANITE as a maintenance treatment in patients with first-line MSS-CRC who have completed FOLFOX (or FOLFOXFIRI)-bevacizumab induction therapy, was announced in late 2021 and the first patient was enrolled in January 2022. Preliminary results from the study are expected in 4Q2023.

Figure 5. Clinical Activity in Previously Treated MSS-CRC Based on Partial and Complete Molecular Responses and Associated Prolonged Progression-Free Survival



SD=stable disease; PD=progressive disease
** ctDNA samples not available; Molecular response is defined as >= 30% decrease in ctDNA from baseline at any post-baseline; ctDNA assessment based on Gritstone-developed, tumor-informed assay.

Figure 6. ctDNA Reduction was Associated with Prolonged Overall Survival in Phase 1/2 trial assessing GRANITE; Median Overall Survival in Molecular Responders Exceeds 22 Months



[1] 13 MSS-CRC patients treated; 2 did not have samples for analysis of ctDNA changes relative to baseline and included in without MR group; 6 of 11 were molecular responders; Molecular responders defined as patients with ≥30% reduction in ctDNA

[2] Mayer et al., The New England Journal of Medicine 372, 1909-1919 (2015)

[3] Grothey et al., The Lancet 381, 303-312 (2013)

Notes: GRTS vaccine candidates have not been studied head-to-head with those listed. Data cut-off: Aug 31, 2022; Molecular response is defined as >= 30% decrease in ctDNA from baseline at any post-baseline; ctDNA assessment based on Gritstone-developed, tumor-informed assay.

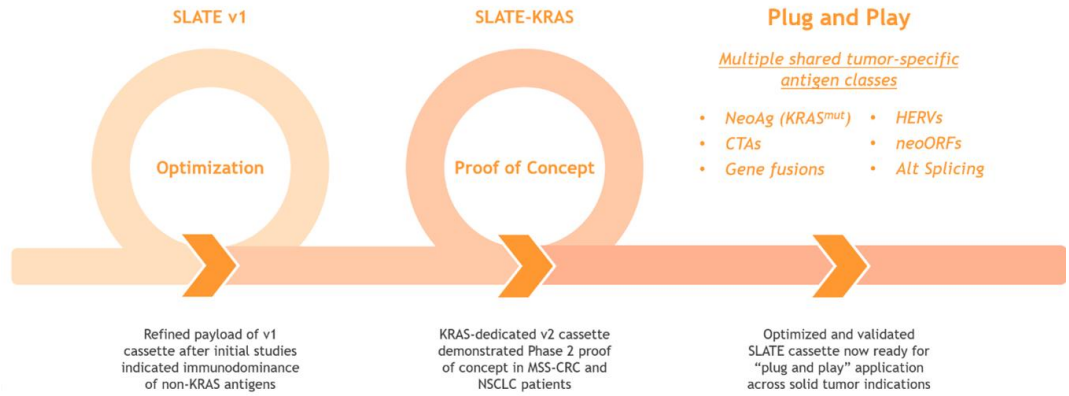
SLATE "off-the-shelf" neoantigen-based immunotherapy vaccine

Our "off-the-shelf" TSNA-directed immunotherapy program, SLATE, utilizes the same heterologous prime-boost approach as GRANITE but contains TSNA that are shared across a subset of cancer patients (rather than TSNA customized for that patient). The key differentiator and advantage of SLATE as compared to GRANITE is speed. SLATE vaccines are produced and delivered to clinical sites proactively and can be administered rapidly upon patient selection (achieved by standard commercial screening for driver mutations). We believe vaccines capable of targeting neoantigens from common tumor driver mutations, such as SLATE, have a clear potential clinical utility and commercialization advantages that are complementary to individualized vaccines.

An initial version of SLATE (SLATE v1) was studied in a Phase 1/2 study in patients with metastatic solid tumors (n = 26). SLATE v1 demonstrated induction of CD8+ T cells against multiple KRAS driver mutations and greatest activity was observed in a subset of NSCLC patients with KRASmut G12C mutations. With these initial data, we developed a second SLATE candidate that exclusively includes epitopes from mutated KRAS (SLATE-KRAS) and evaluated it under the same study protocol. In results shared during ESMO 2022, SLATE-KRAS exhibited immunogenic superiority over v1 in human HLA-transgenic mice and cancer patients, and demonstrated similar molecular response and overall survival trends as those seen in Phase 1/2 study of GRANITE. In 38 patients with advanced solid tumors evaluating both SLATE v1 (n =26) and SLATE-KRAS (n=12), the candidates demonstrated a 39% molecular response rate (MRR) in evaluable patients with MSS-CRC and NSCL and among the 18 patients with NSCLC, a molecular response was correlated with extended median OS (mOS of 9.6 months in molecular responders vs. 4.5 months in non-responders).

We believe the results to date demonstrate our ability to both accurately define shared neoantigen targets and engineer the SLATE cassette and vaccine to optimize immune response based on those specific mutations. Having optimized and validated the SLATE cassette, we now believe the SLATE platform is ready for "plug and play" application across solid tumor indications and shared tumor neoantigen classes. In advancing SLATE, we aim to combine the potential benefits of the full spectrum of tumor antigens with the practicality of the "off-the-shelf" approach.

Figure 7. Off-The-Shelf Immunotherapy Platform, SLATE Ready for Application Across Solid Tumor Indications and Shared Tumor Neoantigen Classes



* CTAs – cancer testis antigens; HERVs – human endogenous retroviruses; neoORFs – noncanonical open reading frames

Infectious Disease Programs

We currently have two clinical-stage infectious disease programs, a collaboration with Gilead Sciences, Inc. (Gilead) to develop a therapeutic vaccine for human immunodeficiency virus (HIV) and CORAL, a second-generation SARS-CoV-2 program. The HIV program represents the first therapeutic application of our platform against an infectious disease. CORAL serves as proof-of-concept for our ability to develop potent, durable self-amplifying mRNA (samRNA) vaccines for prophylactic application.

HIV Vaccine in Collaboration with Gilead Sciences, Inc.

In January 2021, we entered into a collaboration, option and license agreement with Gilead to research and develop a vaccine-based immunotherapy for HIV. Together, we aim to develop an HIV-specific therapeutic vaccine using our proprietary prime-boost vaccine platform, comprised of samRNA and adenoviral vectors, with antigens developed by Gilead. Under the terms of the agreement, Gilead invested $60.0 million, consisting of a $30.0 million upfront cash payment and a $30.0 million equity investment at the closing. Gilead is responsible for conducting a Phase 1 study for the HIV-specific therapeutic vaccine and holds an exclusive option under the collaboration to obtain an exclusive license to develop and commercialize the HIV-specific therapeutic vaccine beyond Phase 1. We are also eligible to receive up to an additional $725.0 million if the option is exercised and if certain clinical, regulatory and commercial milestones are achieved, as well as mid-single-digit to low double-digit tiered royalties on net sales upon commercialization. The HIV program is currently in Phase 1.

CORAL – Second Generation COVID-19 Vaccine Program

The CORAL program was initiated in 2021 in response to emerging limitations of first-generation COVID-19 vaccines, and today, serves as proof-of-concept for our ability to drive more potent and durable responses than those of current vaccines in prophylactic applications. As seen in COVID-19 and other infectious diseases, immune responses can vary, viruses mutate, and neutralizing antibodies wane, necessitating re-dosing (boosters). An approach capable of inducing a potent, broad immune response could have utility across a variety of viral and infectious diseases,

In multiple ongoing Phase 1 trials, we have generated early data demonstrating the potential ability of our vaccines to elicit potent and durable neutralizing antibody responses, and potent cytotoxic cellular responses against Spike and other conserved targets regions of the virus. These results have also provided early signals of the potential advantages of self-amplifying mRNA over first-generation mRNA.

Across the three active Phase 1 trials (CORAL-BOOST, CORAL-CEPI and CORAL-NIH), there are multiple constructs being evaluated with various antigenic cassettes designed to target Wild Type, Beta and Omicron variants. The trials are evaluating our approach in different populations including elderly adults, immunocompromised individuals, those naïve to the virus, and previously

vaccinated individuals using different vaccine regimens. In all, these trials are designed to answer core questions regarding self-amplifying mRNA dose regimen, and the patient populations that could be applicable to other infectious diseases.

We believe that our CORAL vaccine candidates have the potential to improve both B cell and T cell responses to Spike and other viral proteins. By creating a cassette that targets several viral antigens including Spike protein and additional TCE from the SARS-CoV-2 virus, some of which are highly conserved between viral strains (such as SARS and SARS-CoV-2), we believe our vaccine candidates may have pan-coronavirus potential to protect against future coronavirus pandemics. While mutations in the Spike protein may reduce protection by antibodies (since the antibody target changes its shape), broad T cell immunity and long-term memory to different viral proteins may provide a second layer of clinical protection. The CORAL program is supported by the Bill & Melinda Gates Foundation, the Coalition for Epidemic Preparedness Innovation (CEPI) and the National Institute of Allergy and Infectious Diseases (NIAID).

Preclinical Research

Beyond GRANITE, SLATE, CORAL and the HIV collaboration with Gilead, we continue to apply our broad set of capabilities in oncology and infectious diseases through promising preclinical work and partnerships. These projects include development of an optimal immunogen in the context of human papillomavirus (HPV) that is supported by the Gates Foundation. We are also researching the development of an influenza (flu) vaccine and a new combination respiratory vaccine candidate against multiple respiratory viruses.

New Developments

Randomized, Phase 2 Trial in SLATE

In January 2023, we announced plans to initiate a randomized, Phase 2 study evaluating KRAS-directed SLATE in patients with newly diagnosed metastatic cancer. We expect to initiate this randomized study, which is separate from the ongoing Phase 1/2 study in SLATE, in the second half of 2023.

NCI Clinical Trial Collaboration

In February 2023, we entered into a clinical trial agreement with the National Cancer Institute (NCI) to evaluate an autologous T cell therapy expressing a T cell receptor targeting mutated KRAS in combination with Gritstone's KRAS-directed vaccine candidate, SLATE-KRAS in a Phase 1 study.

License and Collaborations

HIV Vaccine in Collaboration with Gilead Sciences, Inc.

In January 2021, we entered into a collaboration, option and license agreement with Gilead to research and develop a vaccine-based immunotherapy for HIV. Together, we aim to develop an HIV-specific therapeutic vaccine using our proprietary prime-boost vaccine platform, comprised of samRNA and adenoviral vectors, with antigens developed by Gilead. Under the terms of the agreement, Gilead invested $60.0 million, consisting of a $30.0 million upfront cash payment and a $30.0 million equity investment at the closing. Gilead will be responsible for conducting a Phase 1 study for the HIV-specific therapeutic vaccine and holds an exclusive option under the collaboration to obtain an exclusive license to develop and commercialize the HIV-specific therapeutic vaccine beyond Phase 1. We are also eligible to receive up to an additional $725.0 million if the option is exercised and if certain clinical, regulatory and commercial milestones are achieved, as well as mid-single-digit to low double-digit tiered royalties on net sales upon commercialization. Gritstone and Gilead received IND clearance for this program in December 2021, and the program is currently in Phase 1.

Strategic Collaboration with 2seventy bio

In August 2018, we entered into a research collaboration and license agreement with bluebird bio, Inc. (bluebird), to utilize our EDGE™ platform to identify and validate tumor-specific targets and provide TCRs directed to 10 selected targets for use in bluebird's cell therapy platform. In November 2021, bluebird assigned the research collaboration and license agreement to its affiliate, 2seventy bio, Inc. (2seventy), in connection with an internal restructuring and subsequent spin-out of 2seventy (such research collaboration and license agreement, as assigned, 2seventy Agreement). In connection with the 2seventy Agreement, we received a non-refundable up-front cash payment of $20.0 million and an additional $10.0 million in equity investment in our Series C convertible preferred stock. We are also eligible to receive up to an aggregate of $1.2 billion in development, regulatory and commercial milestones associated with 2seventy's resulting cell therapy products, as well as tiered, single-digit royalties on sales of the TCR immunotherapy products that

utilize the TCRs discovered by us. The royalty term for each TCR immunotherapy product shall be determined on a product-by-product and country-by-country basis and will commence on the first commercial sale of each product in a country and end on the latest of: (i) expiration or termination of the last to expire valid claim of the last licensed patent that covers the product pursuant to the 2seventy Agreement; (ii) expiration of all periods of regulatory exclusivity for the product in such country (in respect of sales in that country); and (iii) 10 years after the first commercial sale of such product in such country (in respect of sales in that country). 2seventy will be solely responsible for all costs and expenses of its development, manufacturing, and commercial activities for resulting therapies.

The identification, validation, selection and development of the TCRs will be conducted during an estimated 5-year research term and may be extended by an additional year under certain conditions. The collaboration will be governed by a joint steering committee with representatives from Gritstone and 2seventy. We and 2seventy have exchanged non-exclusive licenses to carry out the research program, and, on a selected target-by-selected target basis, we have granted 2seventy an exclusive worldwide license to research, develop, and commercialize resulting cell therapy products directed to such targets, including rights to utilize TCRs discovered by us. The collaboration term ends on a country-by-country and product candidate-by-product candidate basis based on completion of all payments owed to us by 2seventy thereon. Either party may terminate the 2seventy Agreement upon written notice to the other party in the event of the other party's uncured material breach, subject to a dispute resolution process. In addition, 2seventy may terminate the 2seventy Agreement for convenience upon prior written notice to us.

License Agreement with Arbutus Biopharma Corporation and Protiva Biotherapeutics

On October 16, 2017, we executed a license agreement with Arbutus Biopharma Corporation (Arbutus) and Protiva Biotherapeutics and subsequently amended certain terms in July 2018 (such amended license agreement, Arbutus License Agreement). Arbutus is a leader in LNP technology with a broad intellectual property estate and a large library of LNPs, including multiple LNPs being used in clinical development by its partners, as well as the chemistry expertise to synthesize novel LNPs with properties optimal for samRNA.

Under the Arbutus License Agreement, Arbutus granted us a worldwide, exclusive (even as to Arbutus, subject to certain limited exceptions), sublicensable, transferable license, to research, develop, manufacture, and commercialize our novel RNA-based platform for intracellular delivery of samRNA encoding TSNA in combination with one or more of Arbutus' proprietary LNPs. The licensed technology includes Arbutus' portfolio of proprietary and clinically validated LNP products and associated intellectual property and includes technology transfer of Arbutus' manufacturing know-how. Following the execution of the Arbutus License Agreement, we have identified an LNP formulation that we believe will be optimal for use in our GRANITE and SLATE clinical trials. Our goal is to deliver a second-generation samRNA immunotherapy that has the potential to serve as a homologous prime-boost immunotherapy.

Under the Arbutus License Agreement, we paid Arbutus an upfront payment of $5.0 million. We also agreed to make (i) aggregate payments of up to $73.5 million upon the achievement of specified development milestones for up to three products, (ii) an aggregate $50.0 million in commercial milestone payments and (iii) royalty payments in the low single-digits on net sales of licensed products for a royalty term lasting until the expiration of the last patent covered under the Arbutus License Agreement. Following acceptance of our first IND in September 2018, we made the first milestone payment of $2.5 million to Arbutus. In August 2019, a milestone was met following the initial patient treatment of SLATE in our GO-005 clinical trial. In connection with such milestone, we recorded $3.0 million as research and development expenses in 2019 and made the milestone payment in October 2019. Further milestone payments are not expected to occur before 2023.

The Arbutus License Agreement continues in effect until the last to expire royalty payment or early termination. The Arbutus License Agreement is terminable by us for convenience with 60 days prior written notice, upon payment of a no-cause termination sum. We may also terminate it in the event of material adverse safety data for a product, failure to achieve a primary or secondary efficacy endpoint, or if a regulatory authority takes action that prevents us from commercializing any product. Either party may terminate the Arbutus License Agreement for material breach, and Arbutus may terminate it for abandonment or if we challenge Arbutus patents.

License Agreement with Genevant Sciences GmbH

On October 20, 2020, we entered into an Option and License and Development Agreement with Genevant Sciences GmbH (Genevant, and such agreement, 2020 Genevant Agreement). Pursuant to the 2020 Genevant Agreement, Genevant granted us exclusive license rights under certain intellectual property related to Genevant's lipid nanoparticle technology (LNP Technology) for a single indication (HIV), and we agreed to pay Genevant an initial payment of $2.0 million, up to an aggregate of $71.0 million in specified development, regulatory, and commercial milestones, and low to mid-single digit royalties on net sales of licensed products. The 2020 Genevant Agreement expands our intellectual property rights to the LNP technology originally obtained pursuant to our Arbutus License Agreement.

Pursuant to the 2020 Genevant Agreement, Genevant also granted us certain options to expand the licensed field beyond the single indication. If we exercise any options under the 2020 Genevant Agreement to expand the licensed field, we would be required to pay to Genevant additional option exercise fees, certain development, regulatory and commercial milestones and royalties on net sales of licensed products in respect of the expanded licensed field. We also granted Genevant a nonexclusive license to certain intellectual property developed under the Arbutus License Agreement.

The 2020 Genevant Agreement continues in effect until the last to expire royalty term or early termination. The 2020 Genevant Agreement is terminable by us for convenience with 90 days prior written notice or immediately if based on certain product safety or efficacy or regulatory criteria. Either us or Genevant may terminate the 2020 Genevant Agreement for material breach, subject to a cure period, and Genevant may terminate it if we challenge a licensed patent.

License Agreement with Genevant Sciences GmbH

On January 15, 2021, we entered into a Non-Exclusive License and Development Agreement with Genevant (2021 Genevant Agreement). Pursuant to the 2021 Genevant Agreement, we obtained a nonexclusive license to Genevant's LNP Technology to develop and commercialize self-amplifying RNA vaccines against SARS-CoV-2. Further, we (i) agreed to pay Genevant an upfront payment of $1.5 million and (ii) are subject to (x) additional payments up to an aggregate of $141.0 million per product, upon achievement of certain development and commercial milestones and (y) tiered royalties ranging from the mid-single digits to mid-teens on net sales of licensed products for a royalty term lasting until the later of expiration of the last covered patent under the 2021 Genevant Agreement. In certain scenarios, in lieu of milestones and royalties, Genevant will be entitled to a percentage of any amounts that we receive from sublicenses to the COVID-19 program subject to certain conditions. The 2021 Genevant Agreement further expands our intellectual property rights to the LNP technology originally obtained pursuant to the Arbutus License Agreement.

The 2021 Genevant Agreement continues in effect until the last to expire royalty term or early termination. The 2021 Genevant Agreement is terminable by us for convenience with 90 days prior written notice or immediately if based on certain product safety or efficacy or regulatory criteria. Either us or Genevant may terminate the 2021 Genevant Agreement for material breach, subject to a cure period, and Genevant may terminate it if we challenge a licensed patent.

The 2021 Genevant Agreement contains, among other provisions, representation and warranties, indemnification obligations, confidentiality, audit and inspection, and intellectual property sharing provisions in favor of each party that are customary for an agreement of this nature.

CEPI Funding for CORAL Program

In August 2021, CEPI agreed to provide funding of up to $20.6 million to us to advance our CORAL program, with an initial clinical trial of our second-generation COVID-19 vaccine in South Africa. Under the terms of that agreement (CEPI Funding Agreement), CEPI will fund a multi-arm Phase 1 study evaluating the CORAL program's samRNA vaccine in naïve, convalescent, and HIV+ patients. The study initially planned to evaluate two different samRNA vaccine constructs that each target both the spike protein and other SARS-CoV-2 targets and are designed to drive both robust B and T cell immune responses.

The CEPI Funding Agreement also provides for an agreement on the importance of global equitable access to the vaccine produced pursuant to the CEPI Funding Agreement. The vaccine, if approved, is expected to be made available for procurement and allocation to the COVAX Facility, which aims to deliver equitable access to COVID-19 vaccines for all countries, at all levels of development, that wish to participate.

The scope and continuation of the CEPI Funding Agreement may be amended depending on ongoing developments of the COVID-19 outbreak and the success of our COVID-19 vaccine candidate developed under the CEPI Funding Agreement relative to other third-party COVID-19 vaccine candidates or treatments. In December 2021, we and CEPI amended the CEPI Funding Agreement to provide for up to $5 million in additional funding to conduct a Phase 1 clinical trial of the CORAL program's Omicron vaccine candidate in South Africa.

If the World Health Organization (WHO), CEPI or a regulatory authority having jurisdiction over a clinical trial performed under the CEPI Funding Agreement determines that a third-party product candidate has substantially greater potential than the our COVID-19 vaccine candidate developed under the CEPI Funding Agreement and should be prioritized instead for a particular trial, we must consider in good faith any written request of CEPI not to proceed with a clinical trial of such COVID-19 vaccine candidate (the determination of whether to proceed or not with such trial shall be made by us in our sole discretion). In addition, CEPI has the right to unilaterally terminate the CEPI Funding Agreement upon prior written notice if CEPI determines that (i) there are material safety, regulatory, scientific misconduct or ethical issues with the project undertaken by us under the CEPI Funding Agreement, (ii) the project

undertaken by us under the CEPI Funding Agreement must be terminated, (iii) we become unable to discharge its obligations under the CEPI Funding Agreement, (iv) we fail to meet certain criteria set forth in the CEPI Funding Agreement, or (v) we commit fraud or a financial irregularity, as such terms are defined in the CEPI Funding Agreement. Certain termination rights for CEPI are subject to cure periods.

For additional information on all our license and collaboration arrangements, see "*Collaboration and License Agreements*" in Note 7 to our consolidated financial statements.

Manufacturing

Manufacturing is a vital component of our individualized immunotherapy platform, and we are devoting significant resources to manufacturing and process development in an effort to maintain the potential safety and efficacy of our product candidates, as well as to reduce our per-unit manufacturing costs and time to market. The production of our individualized immunotherapy candidates requires two distinct elements for each patient: tumor biopsy analysis to determine candidate neoantigens, followed by manufacture of vectors containing an individualized cassette encoding the selected neoantigens. SLATE and CORAL contains a fixed cassette with TSNA or SARS-CoV-2 vaccine constructs that is shared across cancer patients/subjects rather than a cassette unique to an individual patient, which is designed to provide an off-the-shelf alternative to our individualized manufactured product candidate, GRANITE. The manufacture of these vectors involves complex processes, including per-patient plasmid production, mammalian cell production of virus and RNA synthesis and lipid encapsulation. SLATE and CORAL manufacturing, as a fixed, "off-the-shelf" product candidate, are not time-sensitive and while manufacturing scale differs, both are relatively straightforward operationally. GRANITE, on the other hand, is an "N of 1" product candidate and is manufactured in real-time for each patient, which involves a greater logistical burden.

Our goal is to carefully manage our fixed-cost structure, maximize optionality, and drive long-term cost of goods as low as possible. We have used a hybrid approach to manufacturing and release of our individualized immunotherapy candidates whereby certain elements of our product candidates are manufactured and tested on an outsourced basis at CMOs, and other elements of our product candidates are manufactured and released internally at the 42,600 square foot manufacturing facility we established in 2017 in Pleasanton, California, all designed in compliance with cGMP.

Our manufacturing process begins with receipt of a patient's routine biopsy and blood sample at our Cambridge, Massachusetts facility, where TSNA identification is performed using the EDGE™ platform. The TSNA sequences generated by our platform are sent electronically to our Pleasanton, California manufacturing facility to generate the patient-specific TSNA cassette, which is then cloned into each of the ChAd and samRNA vectors and amplified. Following amplification, the ChAd vector containing the cassette is further manufactured into the final drug product and vialed onsite. In parallel at the Pleasanton facility, the samRNA vector is manufactured into RNA, formulated into LNP, and vialed onsite. Currently, the entire manufacturing process, from biopsy receipt at our facilities to the release and shipment of the individualized immunotherapy candidate to the clinical site for patient administration, often takes approximately 16-20 weeks in principle. Our goal is for this production and release timeline (and associated cost) to diminish over time due to process scaling, potential improvements in production and testing technologies, internal process expertise, internalization of potential reductions in regulatory testing requirements based on clinical experience.

To achieve this, our process development group is focused on several key initiatives. The first is investigating novel approaches to manufacturing our products, including process optimization and quality by design of each intermediate, drug substance and drug product. Additionally, we are systematically characterizing our manufacturing processes, including product intermediates and manufacturing unit operations. This characterization effort is designed to enable us to implement process changes over the entire product lifecycle and to quickly react to evolving process technologies that can lead to reductions in per-unit manufacturing costs and shorter process cycle times. In addition, we plan to establish automated, closed-platform manufacturing processes. Our goal is for these processes to enable us to conduct manufacturing in a lower-classified, lower cost manufacturing environment for multiple steps of our drug product manufacturing.

For our CORAL program, manufacturing of early-stage clinical lots was initiated on our Pleasanton, California manufacturing facility towards the end of 2020 and we have continued to produce next generation, variant-specific clinical lots through 2021 within this facility. Product candidates include both samRNA and adenoviral vectors to deliver SARS-CoV-2 viral antigens. Additional scale-up activities involving CMOs will be needed as the CORAL program progresses leading to large demand for the product candidates.

Our manufacturing strategy is currently structured to support our U.S., E.U., South African, and Australian development plans. We believe this manufacturing strategy developed for global distribution will enable use in other geographies. Specific supply strategies for other geographies will be developed as part of our clinical and commercial plans for such other geographies.

Commercialization Plan

We do not currently have any approved therapies, and we do not anticipate receiving marketing authorization for our early development candidates in either the United States or other worldwide regions in the near future. An internal expansion of sales, marketing, and commercial distribution capabilities would be developed once we have obtained clinical data that can support licensure following discussions with the FDA or other worldwide health authorities. If and when any of our development candidates are approved for commercialization, we intend to create an infrastructure to support ongoing sales in the United States and, possibly in other regions.

Competition

The biotechnology and pharmaceutical industries put significant emphasis and resources into the development of novel and proprietary therapies for treatment of cancer and infectious disease. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions and governmental agencies and public and private research institutions. We anticipate that we will continue to face increasing competition in our field as new therapies, technologies, and data emerge.

In addition to the current standard of care for patients, a number of parties in the field of immunotherapy are pursuing commercial and academic clinical trials. Results from these trials have fueled continued interest in immunotherapy, and our competitors include:

- In the neoantigen space, BioNTech AG (which acquired Neon Therapeutics in May 2020) in collaboration with Genentech Inc., Moderna Therapeutics, Inc. in collaboration with Merck & Co. Inc., Advaxis Immunotherapies, Achilles Therapeutics, Neogene Therapeutics (acquired by Astrazeneca), NousCom AG, Nykode Therapeutics AS in collaboration with Genentech Inc., PACT Pharma, Inc., Transgene SA, and Geneos Therapeutics, Inc.
- In the infectious disease space, Moderna, Pfizer Inc. in collaboration with BioNTech AG, AstraZeneca plc, Johnson & Johnson, Merck, Novavax, Inc., Sanofi, GlaxoSmithKline plc, Arcturus Therapeutics in collaboration with CSL, and CureVac AG.
- In the samRNA space, GlaxoSmithKline plc, Arcturus Therapeutics, Inc., HDT Bio, Corp. and Imperial College London in collaboration with AstraZeneca plc.

Many of our competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and gene therapy 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 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 products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products 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. The key competitive factors affecting the success of our programs are likely to be their efficacy, safety, cost and convenience.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our products and services, to operate without infringing the proprietary rights of others, and to prevent others from infringing our proprietary rights. We rely on a combination of patents and trade secrets, as well as contractual protections, to establish and protect our intellectual property rights. We seek to protect our proprietary position by, among other things, filing patent applications in the United States and internationally. Our patent estate includes patents and patent applications with claims relating to our products, methods, and manufacturing processes, and broader claims for potential future products and developments. As of December 31, 2022, our solely-owned patent portfolio includes, on a worldwide basis, pending patent applications and issued patents relating to our products, methods, and manufacturing processes.

As of December 31, 2022, our solely-owned patent estate includes a portfolio of pending patent applications and issued patents, including those related to our epitope discovery platform, next-generation vectors, and immunogen designs. Details regarding these portfolios are provided below.

As of December 31, 2022, our solely-owned patent portfolio related to our epitope discovery platform , includes domestic and international patent rights with claims related to antigen identification and related compositions, uses and manufacture. Any patents that have or may issue from these patent rights are expected to expire between 2036 and 2043, absent any patent term adjustments or extensions.

As of December 31, 2022, our solely-owned patent portfolio related to our next-generation vectors included domestic and international patent rights with claims related to ChAd- and samRNA-based compositions and their related uses and manufacture. Any patents that have or may issue from these patent rights are expected to expire between 2037 and 2043, absent any patent term adjustments or extensions.

As of December 31, 2022, our solely-owned patent portfolio related to our immunogen designs included domestic and international patent rights with claims related to oncology and infectious disease immunogen and their related uses and manufacture. Any patents that have or may issue from these patent rights are expected to expire between 2039 and 2043, absent any patent term adjustments or extensions.

In addition to patents, we have filed for trademark registration with the United States Patent and Trademark Office (USPTO) as well as certain other international trademark agencies, for “GRITSTONE,” “GRANITE,” “SLATE” and our logo. Furthermore, we rely upon trade secrets, know-how and continuing technological innovation to develop and maintain our competitive position.

In some instances, we submit patent applications directly with the USPTO as provisional patent applications. Provisional applications for patents were designed to provide a lower-cost first patent filing in the United States. Corresponding non-provisional patent applications must be filed not later than twelve (12) months after the provisional application filing date. The corresponding non-provisional application benefits in that the priority date(s) of the patent application is/are the earlier provisional application filing date(s), and the patent term of the finally issued patent is calculated from the later non-provisional application filing date. This system allows us to obtain an early priority date, add material to the patent application(s) during the priority year, obtain a later start to the patent term and to delay prosecution costs, which may be useful in the event that we decide not to pursue examination in an application. We file U.S. non-provisional applications and Patent Cooperation Treaty (PCT) applications that claim the benefit of the priority date of earlier filed provisional applications, when applicable. The PCT system allows a single application to be filed within twelve (12) months of the original priority date of the patent application, and to designate PCT member states in which national patent applications can later be pursued based on the international patent application filed under the PCT. The PCT searching authority performs a patentability search and issues a non-binding patentability opinion which can be used to evaluate the chances of success for the national applications in foreign countries prior to having to incur the filing fees. Although a PCT application does not issue as a patent, it allows the applicant to seek protection in any of the member states through national-phase applications.

At the end of the period of two and a half years from the first priority date of the patent application, separate patent applications can be pursued in any of the PCT member states either by direct national filing or, in some cases by filing through a regional patent organization, such as the European Patent Organization. The PCT system delays expenses, allows a limited evaluation of the chances of success for national/regional patent applications and enables substantial savings where applications are abandoned within the first two and a half years of filing.

For all patent applications, we determine claiming strategy on a case-by-case basis. Advice of counsel and our business model and needs are always considered. We file patents containing claims for protection of all useful applications of our proprietary technologies and any products, as well as all new applications and/or uses we discover for existing technologies and products, assuming these are strategically valuable. We continuously reassess the number and type of patent applications, as well as the pending and issued patent claims to ensure that maximum coverage and value are obtained for our processes, and compositions, given existing patent office rules and regulations. Further, claims may be modified during patent prosecution to meet our intellectual property and business needs.

We recognize that the ability to obtain patent protection and the degree of such protection depends on a number of factors, including the extent of the prior art, the novelty and non-obviousness of the invention, and the ability to satisfy the enablement requirement of the patent laws. The patent positions of biotechnology companies like ours are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted or further altered even after patent issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our product candidates or for our technology platform. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

Our commercial success will also depend in part on not infringing the proprietary rights of third parties. In addition, we have licensed rights under proprietary technologies of third parties to develop, manufacture and commercialize specific aspects of our

products. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, alter our processes, obtain licenses or cease certain activities. The expiration of patents or patent applications licensed from third parties or our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future technology may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO to determine priority of invention.

We further own trade secrets relating to our technology, and we maintain the confidentiality of proprietary information to 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 trade secrets and know-how by entering into confidentiality agreements with third parties, consultants and employees who have access to such trade secrets and know-how. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us are to be kept confidential and not disclosed to third parties except in specific circumstances. In addition, we enter into employment agreements that require employees to assign to us any inventions, trade secrets or know-how that they develop while employed by us. Although we take steps to protect our proprietary information and trade secrets, including through agreements with our employees and consultants, these agreements may be breached, or third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. To the extent that our employees, consultants, scientific advisors or other contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know how and inventions.

For a more comprehensive discussion of the risks related to our intellectual property, please see the section titled "Risk Factors—Risks Related to Intellectual Property."

Government Regulation

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

In the United States, the FDA regulates biologic products under both the Federal Food, Drug and Cosmetic Act (FDCA) and the Public Health Service Act and their respective implementing regulations. Our product candidates are subject to regulation by the FDA as biological products. Biological products require the submission of a biologics license application (BLA) and licensure, which constitutes approval, by the FDA before being marketed in the United States. None of our product candidates has been approved by the FDA for marketing in the United States, and we currently have no BLAs pending. Failure to comply with applicable FDA or other requirements at any time during product development, clinical testing, the approval process or after approval may result in administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, suspension or revocation of approved applications, warning letters, product recalls, product seizures, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution.

The process required by the FDA before biologic product candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND which must become effective before clinical trials may begin;
- approval by an independent Institutional Review Board (IRB) or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials in accordance with the IND, protocol, and FDA's good clinical practice (GCP) regulations to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA after completion of all pivotal clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;

- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites,
- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

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

In addition to the submission of an IND to the FDA before initiation of a clinical trial in the United States, under the National institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines) supervision of human gene transfer trials includes evaluation and assessment by an institutional biosafety committee (IBC) a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Generally, a separate submission to the IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure

For purposes of BLA approval, human clinical trials are typically conducted in three (3) sequential phases that may overlap or be combined.

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

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and they must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the safety, purity and potency. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Submission and Review

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. The submission of a BLA requires payment of a substantial application user fee to the FDA unless a waiver or exemption applies.

Once a BLA has been submitted, within sixty (60) days, the FDA first reviews the BLA to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. Once filed, the FDA's goal is to review standard applications within ten (10) months after the filing date or, if the application qualifies for priority review, six (6) months after the filing date. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites, as well as the sponsor, to assure compliance with GCP.

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

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy (REMS) to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use. A REMS program may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate healthcare providers of the drug's risks, or other elements to assure safe use, such as limitations on who may prescribe or dispense the drug, dispensing only under certain circumstances, special monitoring and the use of patient registries. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. The fast track program is intended to expedite or facilitate the process for reviewing new product candidates that meet certain criteria. Product candidates are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a fast track product candidate has opportunities for frequent interactions with the review team during product development. A fast track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

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

Any marketing application for a biologic submitted to the FDA for approval, including a product candidate with a fast track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition compared to marketed products. Sponsors may also obtain a priority review voucher upon approval of a BLA for certain qualifying diseases and conditions that can be applied to a subsequent BLA submission. Generally, priority review designation means the FDA's goal is to take action on the marketing application within six (6) months of the sixty (60) day filing date, compared with ten (10) months under standard review.

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

In 2017, the FDA established the new regenerative medicine advanced therapy (RMAT) designation as part of its implementation of the 21st Century Cures Act, which was signed into law in December 2016. To qualify for RMAT designation, the product candidate must meet the following criteria: (1) it qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. Like fast track and breakthrough therapy designation, RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate and eligibility for rolling review and priority review. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. Once approved, when appropriate, the FDA can permit fulfillment of post-approval requirements under accelerated approval through the submission of clinical evidence, clinical studies, patient registries, or other sources of real-world evidence such as electronic health records; through the collection of larger confirmatory datasets; or through post-approval monitoring of all patients treated with the therapy prior to approval.

Fast track designation, breakthrough therapy designation, priority review, accelerated approval, and RMAT designation do not change the standards for approval but may expedite the development or approval process. In addition, even if a product candidate qualifies for one or more of these programs, the FDA may later decide that it no longer meets the conditions for designation.

Orphan Drug Designation

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

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, meaning there is no previously approved "same drug" for the same orphan condition, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same drug or biologic for the same orphan disease or indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application fee.

An Eleventh Circuit decision in *Catalyst Pharmaceuticals, Inc. vs. FDA* regarding interpretation of the Orphan Drug Act exclusivity provisions as applied to drugs approved for orphan indications narrower than the drug's orphan designation has the potential to adversely impact whether certain products will be able to obtain approval for the remaining, unapproved designated condition without demonstrating clinical superiority, although FDA has indicated that it does not intend to apply *Catalyst* in other scenarios. A designated orphan drug may not receive orphan drug exclusivity that covers the full approved indication if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Emergency Use Authorization

The Commissioner of the FDA, under delegated authority from the Secretary of Health and Human Services (HHS), may, under certain circumstances in connection with a declared public health emergency, allow for the marketing of a product that does not otherwise comply with FDA regulations by issuing an Emergency Use Authorization (EUA) for such product. Before an EUA may be issued by HHS, the Secretary must declare an emergency based on a determination that public health emergency exists that affects or has the significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents (CBRN), or a specified disease or condition that may be attributable to such CBRN. On February 4, 2020, the HHS Secretary determined that there is such a public health emergency that involves the virus now known as SARS-CoV-2, the virus that causes the COVID-19 infection. Once the determination of the threat or emergency has been made, the Secretary of HHS must then declare that an emergency exists justifying the issuance of EUAs for certain types of products (referred to as EUA declarations). On March 27, 2020, the Secretary of HHS declared, on the basis of his determination of a public health emergency that has the potential to affect national security or the health and security of U.S. citizens living abroad that involves SARS-CoV-2, that circumstances exist justifying authorization of drugs and biologics during the COVID-19 pandemic, subject to the terms of any EUA that is issued.

Once an EUA declaration has been issued, the FDA can issue EUAs for products that fall within the scope of that declaration. To issue an EUA, the FDA Commissioner must conclude that (1) the CBRN that is referred to in the EUA declaration can cause serious or life-threatening diseases or conditions; (2) based on the totality of scientific evidence available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing the disease or condition attributable to the CBRN and that the product's known and potential benefits outweigh its known and potential risks; and (3) there is no adequate, approved, and available alternative to the product. Products subject to an EUA must still comply with the conditions of the EUA, including labeling and marketing requirements. Moreover, the authorization to market products under an EUA is limited to the period of time the EUA declaration is in effect, and the FDA can revoke an EUA in certain circumstances.

Post-Approval Requirements

Any products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences and significant interruptions in manufacturing, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which FDA assesses an annual program fee for each product

identified in an approved BLA. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon BLA sponsors and any third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

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

- restrictions on the marketing or manufacturing of a product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are for uses of the product approved by the FDA, that are considered consistent with the approved label, and for which the company has appropriate substantiation, as applicable. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses or promotion that is otherwise false or misleading. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested 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.

Biosimilars and Reference Product Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively ACA) signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCIA) which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered to a patient more than once, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four (4) years following the date that the reference product was first licensed by the FDA. In addition, the FDA may not approve a biosimilar product until twelve (12) years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves an original BLA containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of the competing product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

FDA Regulation of Companion Diagnostics

Our product candidates may require use of an in vitro diagnostic to identify appropriate patient populations. These diagnostics, often referred to as companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, pre-clinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, companion diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval (PMA).

If use of companion diagnostic is essential to safe and effective use of a biologic product, then the FDA generally will require approval or clearance of the diagnostic contemporaneously with the approval of the therapeutic product. On August 6, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance, for novel candidates such as our product candidates, a companion diagnostic device and its corresponding drug or biologic candidate should be approved or cleared contemporaneously by FDA for the use indicated in the therapeutic product labeling. The guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a drug generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption (IDE) regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a drug are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE. In July 2016, the FDA issued a draft guidance document intended to further assist sponsors of therapeutic products and sponsors of in vitro companion diagnostic devices on issues related to co-development of these products.

The FDA generally requires companion diagnostics intended to select the patients who will respond to treatment to obtain approval of a PMA for that diagnostic contemporaneously with approval of the therapeutic. The review of these in vitro companion diagnostics in conjunction with the review of biologics involves coordination of review by the FDA's Center for Drug Evaluation and Research and by the FDA's Center for Devices and Radiological Health. The PMA process, including the gathering of clinical and pre-clinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are also subject to an application fee. In addition, PMAs for certain devices must generally include the results from extensive pre-clinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, the applicant must demonstrate that the diagnostic produces reproducible results when the same sample is tested multiple times by multiple users at multiple laboratories. In addition, as part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution.

If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing. PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the U.S.

Government Regulation Outside of the United States

In addition to regulations in the United States, we may be subject to a variety of regulations in other jurisdictions, including the European Union, governing, among other things, clinical trials, marketing authorizations, post-marketing authorization requirements and any advertising, promotion, commercial sales and distribution of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Ethical, social and legal concerns about gene-editing technology, gene therapy, genetic testing and genetic research could result in additional regulations restricting or prohibiting the processes we may use. Whether or not we obtain FDA approval of a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Non-clinical studies and clinical trials

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

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

Clinical trials of medicinal products in the European Union must be conducted in accordance with EU and national regulations and the International Conference on Harmonization (ICH) guidelines on GCPs, as set out in EU Commission Implementing Regulation (EU) 2017/556, EU Regulation (EU) 2016/679, or GDPR, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of advanced therapy medicinal products (ATMPs). If the sponsor of the clinical trial is not established within the European Union, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation (CTR), which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the European Union via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application (CTA) to be submitted in each member state, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each

member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors were still able to choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those are governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with GMP, as set out in EU Commission Delegated Regulation (EU) 2017/1569. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorization

In order to market our future product candidates in the European Union, and in many other foreign jurisdictions, we must obtain separate regulatory approvals. In the European Union, medicinal product candidates can only be commercialized after obtaining a marketing authorization (MA). To obtain regulatory approval of a product candidate (including an investigational biological product) under EU regulatory systems, we must submit a marketing authorization application (MAA). The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAAs:

- "Centralized MAAs" are issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA), and is valid throughout the European Union. It is compulsory for certain types of product candidates, such as (i) medicinal products derived from biotechnological processes, (ii) designated orphan medicinal products, (iii) ATMPs such as gene therapy, somatic cell-therapy or tissue-engineered medicines and (iv) medicinal products containing a new active substance indicated for the treatment of HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for any other products containing new active substances not authorized in the European Union or for product candidates which constitute a significant therapeutic, scientific, or technical innovation or for which the granting of authorization would be in the interests of public health in the European Union.

  The Committee for Advanced Therapies (CAT), is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CAT is primarily responsible for the scientific evaluation of ATMPs and prepares a draft opinion on the quality, safety and efficacy of each ATMP for which an MAA is submitted. The CAT's opinion is then taken into account by the CHMP when giving its final recommendation regarding the authorization of a product in view of the balance of benefits and risks identified. Although the CAT's draft opinion is submitted to the CHMP for final approval, the CHMP may depart from the draft opinion, if it provides detailed scientific justification. The CHMP and CAT are also responsible for providing guidelines on ATMPs and have published numerous guidelines, including specific guidelines on gene therapies and cell therapies. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in a marketing authorization application; and post-approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions of ATMPs.

- "National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the Mutual Recognition Procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the Reference member state.

Under the centralized procedure, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days. In exceptional cases, the CHMP might perform an accelerated review of an MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines (PRIME), which provides incentives similar to the breakthrough therapy designation in the United States. In March 2016, the EMA launched a PRIME scheme as a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible

for accelerated assessment, but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Moreover, in the European Union, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions ("specific obligations"). Once the pending specific obligations are fulfilled, it can become a "standard" MA. However, if the specific obligations are not fulfilled within the timeframe set by the EMA, the European Commission may, based on a scientific recommendation by the EMA, refuse to renew the MA. Furthermore, MA may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of an MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the European Commission may, based on a scientific recommendation by the EMA, revoke the MA in case the risk-benefit ratio is no longer favorable.

MAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance.

The European Commission is expected to publish new proposed legislation in March 2023 which, if adopted by the European Parliament and the Council of Ministers, will introduce significant number of changes to the regulatory procedures described above. This may potentially affect the MA renewal procedure and the internal organization of the EMA (disbanding of CAT).

Data and marketing exclusivity

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

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

In March 2023, the European Commission is expected to publish new proposed legislation. If adopted by the European Parliament and the Council of Ministers, this legislation will introduce new data and market exclusivity periods which are likely to include additional requirements and modulation mechanisms. Moreover, it is possible that the proposed legislation also foresees a potential reduction in regulatory requirements for the grant of MA for generics and biosimilars.

Orphan Medicinal Products

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

In the European Union, an application for designation as an orphan product can be made any time prior to the filing of the application for MA. Orphan drug designation entitles a party to incentives such fee reductions or fee waivers, protocol assistance, and access to the centralized procedure. Upon grant of an MA, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication, which means that the regulatory authorities cannot accept another MAA, grant an MA, or accept an application to extend an MA for a similar product for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan (PIP). No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The orphan exclusivity period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for which it received orphan drug destination, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity, or where the prevalence of the condition has increased above the threshold. Granting of an authorization for another similar orphan medicinal product where another product has market exclusivity can happen at any time if: (i) the second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior, (ii) inability of the applicant to supply sufficient quantities of the orphan medicinal product or (iii) where the applicant consents to a second orphan medicinal product application. A company may voluntarily remove a product from the orphan register.

The European Commission is expected to publish new proposed legislation in March 2023 which, if adopted by the European Parliament and the Council of Ministers, will introduce significant number of changes to the market exclusivities granted to orphan medicinal products and the related procedures and requirements.

Pediatric Development

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

Post-Approval Requirements

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports (PSURs).

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

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the European Union. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another. A new legislative proposal by the European Commission expected to be published in March 2023 is likely to contain new proposed rules restricting comparative advertising of medicinal products in the EU.

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

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, suspension of the conduct of clinical trials, rejection of clinical trial data, or refusal to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal, revocation or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom left the European Union on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the United Kingdom during the transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the European Union on behalf of its members. The transition period provided time for the United Kingdom and European Union to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement (TCA) and became effective on the January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as “retained EU law”. However, new legislation such as the EU CTR will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an ‘appropriate authority’ to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) is the UK’s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland (Great Britain); broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a guidance on how various aspects of the UK regulatory regime for medicines will operate in Great Britain and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, importing, exporting, and pharmacovigilance and is relevant to any business involved in the research, development, or commercialization of medicines in the United Kingdom. The new guidance was given effect via the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019 (Exit Regulations).

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in Great Britain (only), free of charge on January 1, 2021, unless the MA holder chooses to opt-out. In order to use the centralized procedure to obtain an MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore, after Brexit, companies established in the United Kingdom can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to obtain a UK MA to commercialize products in the UK, an applicant must be established in the United Kingdom and must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the United Kingdom. The MHRA may rely on a decision taken by the European Commission on the approval of a new (centralized procedure) MA when determining an application for a Great Britain authorization or use the MHRA’s decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in Great Britain.

There will be no pre-MA orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market (i.e., the prevalence of the condition in Great Britain, rather than the European Union, must not be more than five in 10,000). Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in Great Britain.

Regulation of Companion Diagnostics

In the European Union, in vitro diagnostic medical devices (IVDs) were regulated by Directive 98/79/EC (the Directive) which regulates the placing on the market, the CE marking, the essential requirements, the conformity assessment procedures, the registration obligations for manufactures and devices as well as the vigilance procedure. In vitro diagnostic medical devices were required to comply with the requirements provided for in the Directive, and with further requirements implemented at national level (as the case may be). For certain IVDs, compliance with the essential requirements was subject to assessment by a notified body. Notified bodies are entities designated by the relevant NCAs and are responsible for assessing the conformity of IVDs before they are placed on the EU market. Under the Directive, the majority of IVDs could be placed on the market as a result of the manufacturer self-certifying the IVD as being in conformity with the essential requirements, without the involvement of a Notified Body.

The Directive was replaced by the Regulation (EU) 2017/746 of the European Parliament and of the Council on in vitro diagnostic medical devices (EU IVDR) that entered into force in May 2017, and which initially included a 5-year transition period until its original effective date of May 26, 2022. Unlike the Directive, that specifies certain requirements that must be achieved by each Member State and permits each Member State to decide how to transpose the Directive into national law to meet those requirements, the IVDR has direct binding legal force throughout every Member State without the need for national implementation. However, due to multiple challenges to the EU IVDR being ready for full application by the May 2022 implementation date, Regulation (EU) 2022/112 of the Parliament and of the Council was published on 25 January 2022 allowing for a delay to the application of the IVDR by amending the transition provision for certain in vitro diagnostic medical devices. For products classified as Class C under the IVDR, the transition period allows for legacy devices with a valid declaration of conformity drawn up prior to May 26, 2022 to continue to be placed on the market until May 26, 2026. However, certain IVDR requirements, including post-market surveillance, market surveillance, vigilance, and registration of economic operators and devices remained effective on the May 26, 2022 implementation date.

The EU IVDR introduces a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue a CE certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or an MAA for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a national competent authority or the EMA.

Other Healthcare Laws and Compliance Requirements

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business, which may constrain the financial arrangements and relationships through which we and our partners research, sell, market and distribute any products for which we obtain marketing approval. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, and transparency laws regarding drug pricing and payments and other transfer of value to physicians and other healthcare providers. If their operations are found to be in violation of any of such laws or any other governmental regulations that apply, they may be subject to penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, including consumer protection laws and regulations, govern the collection, dissemination, use, access to, confidentiality and security of personal information, including health-related information. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and state consumer protection laws and regulations (e.g., Section 5 of the FTC Act), that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data in certain circumstances, many of

which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological product for which we obtain regulatory approval. Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical or biological products, medical devices and medical services, in addition to questioning safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product. No regulatory authority has granted approval for a individualized cancer immunotherapy based on a vaccine approach, and there is no model for reimbursement of this type of product.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of reform proposals to change the healthcare system. There is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by federal and state legislative initiatives, including those designed to limit the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded health care programs, and increased governmental control of drug pricing.

In March 2010, the ACA was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States, and significantly affected the pharmaceutical industry. The ACA contains a number of provisions of particular import to the pharmaceutical and biotechnology industries, including, but not limited to, those governing enrollment in federal healthcare programs, a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Since its enactment, there have been judicial, Congressional, and executive branch challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed a most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace from February 15, 2021 through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted, including aggregate reductions of Medicare payments which went into effect April 1, 2013 and will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 unless additional Congressional action is taken.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries, hearings and proposed and enacted federal legislation and rules, as well as Executive Orders, designed to, among other things, reduce or limit the prices of drugs and make them more affordable for patients, such as by tying the prices that Medicare reimburses for physician-administered drugs to the prices of drugs in other countries, reform

the structure and financing of Medicare Part D pharmaceutical benefits, including through increasing manufacturer contributions to offset Medicare beneficiary costs, bring more transparency to drug pricing rationale and methodologies, enable the government to negotiate prices for drugs covered under Medicare, revise rules associated with the calculation of Medicaid Average Manufacturer Price and Best Price, including removing the current statutory 100% of Average Manufacturer Price per-unit cap on Medicaid rebate liability effective January 1, 2024, which may significantly affect the amount of rebates paid on prescription drugs under Medicaid, and facilitate the importation of certain lower-cost drugs from other countries. More recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, went into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023) and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates.

Our Interactions with the Regulatory Health Authorities

EDGE Development

In two separate FDA interactions, the FDA advised us that our machine-learning software will not be subject to medical device diagnostic regulations. In August 2016, the FDA's Center for Devices and Radiological Health, determined that the TSNA prediction software is a Non-Significant Risk (NSR), device, and that an IDE submission was not required to conduct clinical studies with our product candidate. In April 2017, the FDA's Center for Biologics Evaluation and Research (CBER) confirmed that medical device diagnostic regulations did not apply to our testing and processing of the patient-specific TSNA, and that quality requirements could be met through compliance with biologic cGMPs. Based on these interactions, we believe no additional device-related regulatory submissions (such as an investigational device exemption or pre-market approval application) or device development activities are required, and our TSNA prediction software procedure will be regulated as part of our cGMP manufacturing process.

GRANITE Development Program

Preclinical Safety

In a Pre-IND interaction with the FDA's CBER Office of Tissues and Advanced Therapies (OTAT) the FDA advised us that a single toxicological animal study with a representative vector could be able to support preclinical safety for purposes of IND submission. Subsequent to this discussion, we submitted proposed protocols for GLP toxicology and biodistribution studies for OTAT's review in connection with a Pre-IND meeting, and OTAT confirmed that a single GLP toxicology study could support IND submission. In this GLP toxicology study, we administered our ChAd and the samRNA vectors to Indian Rhesus macaques. The heterologous prime-boost immunotherapy approach when administered intramuscularly was well tolerated at the clinical maximal dose of each platform, with some animals presenting flu-like symptoms. Preclinical chemistry findings included a transient increase in select cytokines, which resolved rapidly.

Clinical Regulatory

In our GRANITE Pre-IND meeting with OTAT the FDA previewed Clinical Protocol GO-004 and confirmed that the overall design appeared reasonable, while providing comments on the study populations and dose determination which we incorporated into the Phase1/2 protocol. OTAT also concurred with our dose limiting toxicity assessment criteria, but reserved comment on the starting dose and dose escalation pending the completion of planned preclinical studies. We intend to include these elements in the protocol, which we believe may permit a faster progression and fewer patients to reach the clinical protocol's combination cohort (Phase 1, Part C).

In our Type-C meeting with OTAT, the FDA reviewed the Phase 2/3 clinical study design for the planned study evaluating first-line maintenance in patients with MSS CRC and discussed approaches for a registrational path. We believe we have aligned with the

FDA to conduct a combined, yet regulatorily and statistically distinct Phase 2/3 clinical study. Molecular response is the primary endpoint for the phase 2 component of the trial, an exploratory efficacy endpoint in the FDA's view. We expect that preliminary Phase 2 data, including molecular response, RECIST radiologic response and Progression-Free Survival (utilizing iRECIST/iPFS as well as RECIST/PFS), together with available ctDNA data will be previewed with the FDA in a subsequent meeting. We expect that the MSS-CRC patient population will be defined with local testing to exclude MSI-Hi patients, with reference data characterizing the expected negligible contributory effect of PD-(L)1/ipilimumab in combination with GRANITE.

Regulatory Chemistry, Manufacturing & Controls

In a Type-C Facilities meeting with the FDA's CBER Division of Manufacturing and Product Quality (DMPQ) we obtained FDA feedback on our then-proposed design for the multi-use clinical manufacturing facility in Pleasanton, California. Importantly, the FDA concurred with our plan to build a facility designed to accommodate manufacture of multiple patient-specific lots in parallel within the same manufacturing suite, which we expect will provide a substantial increase in scalability within a smaller allocation of cleanrooms.

At our subsequent GRANITE Pre-IND meeting with OTAT, the FDA concurred with our proposed use of select rapid release testing methods in which we proposed replacing standard cell-culture based tests with faster polymerase chain reaction methods. As discussed with the FDA, we submitted qualification of these methods in our IND submission for GRANITE. The FDA also found our proposed stability program to be generally acceptable to support the then-proposed Phase 1 clinical study of GRANITE, where only one representative patient lot per year was placed on product stability during conduct of the clinical program.

In support of transitioning the GRANITE manufacturing process from external contract manufacturing organizations to Our Pleasanton manufacturing facility, an IND amendment was submitted to the FDA outlining the Chemistry, Manufacturing, and Controls documentation changes for the ChAd and samRNA product candidates. These revisions included a plasmid backbone change for the samRNA vector and a process improvement for the samRNA drug substance. These updates have been implemented and are currently being utilized in our Pleasanton manufacturing facility.

In our Type-C meeting with OTAT, the FDA clarified phase appropriate CMC requirements to support advancement into late clinical development. The FDA detailed qualification efforts for bioinformatics, manufacturing, and testing to be submitted prior to initiation of the Phase 2 and Phase 3 portions of the Phase 2/3 clinical study. These include providing bioinformatics documentation, qualification of critical analytical assays which include a robust potency assay, as well as materials to support manufacturing process improvements being implemented for GRT-C901 and GRT-R902. We expect that a comprehensive review of CMC will occur in a subsequent pre-Phase 3 meeting with the FDA.

GRANITE Regulatory Milestones

The FDA allowed IND for GRANITE to proceed in September 2018. In December 2018, the FDA granted fast track designation to GRANITE for the treatment of colorectal cancer.

SLATE Development Program

Preclinical Safety

In pre-IND communications with the FDA, following a justification of comparability of ChAd and samRNA products, we received feedback from the FDA noting that pre-clinical pharmacology, pharmacokinetic, and toxicology studies conducted in support of the GRANITE IND, could be used to support the initiation of the clinical study proposed under the SLATE IND. In follow-up correspondence, the FDA requested additional safety pharmacology information on the general anticipated immunogenicity and auto-reactivity elicited with each of the 20 neoantigens expressed in the SLATE cassette, as well as the impact of order and orientation of the neoantigens within the expression cassette.

Clinical Regulatory

In our SLATE Pre-IND communication with OTAT the FDA previewed Clinical Protocol NCT03953235, GO-005 and confirmed that the overall design appeared reasonable, but requested we add language to clarify our proposed dose escalation and stopping rules. The FDA had additional questions on our proposed Next Generation Sequencing method to screen patients for their HLA type and communicated that this novel method may be viewed as a companion diagnostic.

Regulatory Chemistry, Manufacturing & Controls

Much of the manufacturing process contained in SLATE was similar to that used in the GRANITE IND, therefore, the FDA's pre-IND feedback focused primarily on the quality of the reagents, drug product characterization and release, and ongoing stability requests. The FDA inquired on the status of certain research-grade reagents and reminded us of the need to progress to GMP grade materials in the manufacture drug product by the time of BLA approval and commercial licensure. In order to retain consistency in the manufactured drug product across SLATE batches, we were asked to amend the specification of certain release assays' criteria and continue the development of quantitative potency assays for the ChAd and samRNA products prior to approval, and we were asked to summarize our QC plan to prevent, detect, and correct deficiencies that may compromise product integrity or function, or that may lead to the possible transmission of adventitious infectious agents. Additionally, the FDA provided feedback on the proposed method for qualifying Gritstone's proposed accelerated adventitious agent release assay.

SLATE Regulatory Milestones

The FDA allowed our IND for SLATE to proceed in June 2019.

CORAL Development Program

A pre-IND interaction with the FDA was conducted to review the proposed clinical investigation of ChAd vectors encoding the SARS-CoV-2 and CD8+ T-cell epitope spike antigen sequences in normal healthy subjects. The FDA concluded that the overall manufacturing and release testing for the CORAL vaccines candidates, which is similar to the GRANITE/SLATE process, appeared acceptable and requested detail on the transfection process, grade of materials, and release tests be submitted in the IND. We also received feedback that pre-clinical pharmacokinetic, and toxicology studies conducted in support of the GRANITE IND could be used to support the safety information needed to initiate the SARS-CoV-2 clinical study, and that additional animal immune response pharmacodynamic data would be submitted within the IND. The FDA previewed the proposed clinical protocol, confirmed that the overall design appeared reasonable and requested we include language to clarify dose escalation, stopping rules and a sentinel arm. The FDA requested that we exclude those subjects who are being treated with COVID-19 investigational agents or who have a high risk of potential exposure to SARS-CoV-2.

CORAL Regulatory Milestones

In March 2021, the FDA acknowledged our biologics master file which provides CMC and non-clinical sections support of NIH's IND to study CORAL program candidates in previously vaccinated healthy volunteers.

In August 2021, the MHRA provided a notice of acceptance for our CTA to initiate a clinical study of certain CORAL program candidates to boost vaccinate healthy volunteers >60 years in the UK.

In December 2021, the MHRA provided a notice of acceptance for our CTA to initiate a clinical study of certain CORAL program candidates in previously vaccinated B-cell deficient subjects in the UK.

South Africa's SAHPRA provided a notice of acceptance for our CTA to initiate a clinical study to test certain CORAL program candidates in COVID-19 naïve, convalescent, and HIV subjects in South Africa.

In July 2022, Gritstone held a Scientific Advice meeting with the MHRA to discuss the importance of cellular immunity for the development of a COVID vaccine. The MHRA agreed that in principle, T cells could be important for protection against viral infection. The MHRA also acknowledged that T cell responses to non-spike epitopes may create an advantage for protection against new variants and potentially increase durability. The MHRA also agreed that T cell data may be included in the summary of product characteristics.

Financial Information About Segments

We manage our operations as a single reportable segment for the purposes of assessing performance and making operating decisions. See "*Note 2. Summary of Significant Accounting Policies*" in the notes to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Employees

As a mission-driven organization, we value and foster a culture of collaboration, discovery and passion, which is reflected in our hiring and retention strategies. We employ talented individuals who have the skills and expertise to meet the challenges of our mission, and we recognize that our employees are key to our success. Our human capital objectives include hiring goals set to provide us with necessary expertise, integrating new employees, and retaining, incentivizing and developing our existing employees.

As of December 31, 2022, we had 233 full-time employees, including a total of 54 employees with M.D. or Ph.D. degrees. Within our workforce, 100 employees are engaged in research and development, 85 in manufacturing and quality, and 48 are engaged in business development, finance, legal, human resources, facilities, information technology and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Corporate Information

We were founded in August 2015 as a Delaware corporation. In May 2021, we changed our name from Gritstone Oncology, Inc. to Gritstone bio, Inc. Our principal executive offices are located at 5959 Horton Street, Suite 300, Emeryville, California 94608, and our telephone number is (510) 871-6100. Our website address is www.gritstonebio.com. The information on, or that can be accessed through, our website is not part of this report and is not incorporated by reference herein. We have included our website address as an inactive textual reference only. We also use our website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD.

We file electronically with the SEC our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Exchange Act. We make available on our website at www.gritstonebio.com, free of charge, copies of these reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The public may read or copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that website is www.sec.gov. The information in or accessible through the SEC and our website or social media sites does not constitute part of this Annual Report on Form 10-K or any other report or document we file with the SEC, and any references to our website and social media sites are intended to be inactive textual references only.

We use Gritstone bio, Inc.®, the Gritstone bio logo, and other marks as trademarks in the United States and other countries. This Annual Report on Form 10-K contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report on Form 10-K, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by any other entity.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

Summary of Principal Risks Associated with Our Business

- We are a biotechnology company with a limited operating history and no products approved for commercial sale. We have incurred significant losses since our inception, and we anticipate that we will continue to incur significant losses for the foreseeable future, which, together with our limited operating history, makes it difficult to assess our future viability;
- Clinical development involves a lengthy and expensive process with an uncertain outcome, and delays can occur for a variety of reasons outside of our control, including external factors that may affect our clinical trial enrollment;

- We will require substantial additional financing to achieve our goals, and a failure to obtain such necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development programs, commercialization efforts or other operations;

- Our immunotherapy approach is based on novel ideas and technologies that are unproven and may not result in marketable products, which exposes us to unforeseen risks and makes it difficult for us to predict the time and cost of product development and potential for regulatory approval;

- Our business remains highly dependent on the successful development, regulatory approval and commercialization of our individualized immunotherapy product candidate and GRANITE, our "off-the-shelf" immunotherapy product candidate, SLATE, which are in clinical trials;

- We may be unable to obtain regulatory approval for our product candidates under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of our product candidates and adversely impact our potential to generate revenue, our business and our results of operations;

- We rely, and intend to rely, on third parties in the conduct of our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, fail to comply with applicable regulatory requirements, or fail to meet expected deadlines, we may be unable to obtain regulatory approval for our immunotherapy product candidates;

- We currently perform the majority of the manufacturing of our product candidates internally and rely on qualified third parties to supply some components of our product candidates. Our inability to manufacture sufficient quantities of GRANITE, SLATE or any other current or future product candidates, or the loss of our third-party suppliers, or our or their failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, would materially adversely affect our business;

- We face significant competition in an environment of rapid technological and scientific change, and our failure to effectively compete may prevent us from achieving significant market penetration. Most of our competitors have significantly greater resources than we do, and we may not be able to successfully compete;

- Our success depends on our ability to protect our intellectual property and our proprietary technologies and to avoid infringing the rights of others; and

- Our stock price is volatile, and you may not be able to resell shares of our common stock at or above the price you paid.

Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements

We are a biotechnology company with a limited operating history and no products approved for commercial sale. We have incurred significant losses since our inception, and we anticipate that we will continue to incur significant losses for the foreseeable future, which, together with our limited operating history, makes it difficult to assess our future viability.

Product development in the biotechnology industry is a highly speculative undertaking and involves a substantial degree of risk. We are a clinical-stage biotechnology company with a limited operating history upon which you can evaluate our business and prospects. We have no products approved for commercial sale, have not yet generated any revenue from product sales and have incurred losses in each year since our inception in August 2015. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval and become commercially viable. In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, ,complications, delays and other known and unknown factors and risks frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields.

We have had significant operating losses since our inception (for additional information, see "Liquidity" in Note 1 to our consolidated financial statements). Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Our programs will require substantial additional development time and resources before we (or our collaboration partners) would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. In addition, we incur substantial costs associated with operating as a public company. We also do not yet have a sales organization or commercial infrastructure and, accordingly, if our product candidates are approved, we will incur significant expenses to develop a sales organization or commercial infrastructure in advance of generating any commercial product sales. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses

will increase as we continue to develop our current and any future immunotherapy product candidates, conduct clinical trials and pursue research and development activities. Even if we achieve profitability at some point in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We will require substantial additional financing to achieve our goals, and a failure to obtain such necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development programs, commercialization efforts or other operations.

Since our inception, we have invested a significant portion of our efforts and financial resources in research and development activities for tumor-specific cancer immunotherapies and infectious disease programs in addition to establishing our in-house manufacturing capabilities. Our preclinical studies, clinical trials and additional research and development activities will require substantial funds to complete. We believe that we will continue to expend substantial resources for the foreseeable future in connection with the development of our current and any other future immunotherapy product candidates we may choose to pursue, as well as the continued development of our manufacturing capabilities and other corporate uses. Specifically, in the near term, we expect to incur substantial expenses as we advance GRANITE and SLATE through clinical development, seek regulatory approval, prepare for and, if approved, proceed to commercialization, continue our research and development efforts and invest in our manufacturing facility. These expenditures will include costs associated with conducting preclinical studies and clinical trials, obtaining regulatory approvals, and manufacturing and supply, as well as marketing and selling any products approved for sale. In addition, other unanticipated costs may arise. Because the outcome of any of our preclinical studies or clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of GRANITE, SLATE or any other current or future immunotherapy product candidates.

We believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our planned operations for at least twelve (12) months. However, our operating plans and other demands on our capital resources may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations. If we raise additional funds through licensing or collaboration arrangements with third parties, we may have to relinquish valuable rights to our product candidates or grant licenses on terms that are not favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all.

Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of developing each of our product candidates, including conducting preclinical studies and clinical trials, either on our own or in collaboration with others;
- potential delays in our ongoing clinical trials, including for reasons beyond our control;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates;
- the number and characteristics of any additional product candidates we develop or acquire;
- the timing and amount of any milestone, royalty or other payments we are required to make pursuant to any current or future collaboration or license agreement;
- the cost of manufacturing any of our products we successfully commercialize, including the cost of scaling up our internal manufacturing operations;
- the cost of building a sales force in anticipation of product commercialization;
- the cost of commercialization activities, including legal, compliance, marketing, sales and distribution costs;
- our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements and the financial terms of any such arrangement, including the timing and amount of any future milestone, royalty or other payments due under any such arrangement;

- any product liability or other lawsuits related to our products;
- the expenses needed to attract, hire and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property portfolio; and
- the timing, receipt and amount of sales of our future approved products, if any.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to:

- delay, limit, reduce or terminate preclinical studies, clinical trials or other research and development activities or eliminate one or more of our development programs altogether; or
- delay, limit, reduce or terminate our efforts to establish manufacturing and sales and marketing capabilities or other activities that may be necessary to commercialize our immunotherapy product candidates, or reduce our flexibility in developing or maintaining our sales and marketing strategy.

We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights or jointly own some aspects of our technologies or product candidates that we would otherwise pursue on our own. We may not realize revenue from sales of products or royalties from licensed products in the foreseeable future, and no such revenue will be realized unless and until a product candidate is clinically tested, approved for commercialization and successfully marketed. To date, we have primarily financed our operations through the sale of equity securities. We will be required to seek additional funding in the future and currently intend to do so through collaborations, public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these funding sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, is likely to involve restrictive covenants, repayment obligations, or other similar restrictions that may affect our business and limit our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations.

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are beyond our control and may be difficult to predict, including:

- the timing and cost of, and level of investment in, research, development and commercialization activities, which may change from time to time;
- the timing of receipt of approvals from regulatory authorities in the United States and internationally;
- the timing and status of enrollment for our clinical trials;
- the cost of manufacturing, as well as building out our supply chain, which may vary depending on the quantity of production, the cost of continuing to establish and scale up our internal manufacturing capabilities, and the terms of any agreements we enter into with third-party suppliers;
- the timing and amount of any milestone, royalty or other payments due under any current or future collaboration or license agreement;

- coverage and reimbursement policies with respect to our immunotherapy product candidates, if approved, and potential future drugs that compete with our products;

- expenditures that we may incur to acquire, develop or commercialize additional products and technologies;

- the level of demand for our immunotherapy products, if approved, which may vary significantly over time;

- the timing and success or failure of preclinical studies and clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners; and

- future accounting pronouncements or changes in our accounting policies.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any revenue or earnings guidance we previously provided.

Risks Related to Our Business

Our business is highly dependent on the successful development, regulatory approval and commercialization of our product candidates, primarily our individualized immunotherapy product candidate, GRANITE, and our "off-the-shelf" immunotherapy product candidate, SLATE, which are in clinical trials.

We currently have no products approved for sale and may never be able to develop marketable products. All three of our clinical programs are in either Phase 1 or Phase 2 clinical trials. As such, we face significant clinical risk with our programs and our tumor and viral-specific immunotherapy approach generally. The success of our business, including our ability to finance our operations and generate any revenue in the future, will primarily depend on the successful development, regulatory approval and commercialization of GRANITE and SLATE, as well as other product candidates derived from our immunotherapy approach, which may never occur. To date, our product candidates have only been tested in a small number of humans, and, given our early stage of development, it may be many years, if at all, before we have demonstrated the safety and efficacy, especially of an individualized immunotherapy treatment, sufficient to warrant approval for commercialization. In the future, we may also become dependent on other product candidates that we may develop or acquire.

We have not previously submitted a BLA to the FDA or made a similar filing seeking regulatory approval to comparable foreign authorities, for any product candidate, and we cannot be certain that our product candidates will be successful in clinical trials or receive regulatory approval. Further, any product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approvals to market a product candidate, our revenue will be dependent, in part, upon a number of factors outside of our control, including, in particular, the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets or patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved.

We plan to seek regulatory approval to commercialize our product candidates both in the United States and in selected foreign countries. While the scope of regulatory approval generally is similar in other countries, to obtain separate regulatory approval in other countries we must comply with numerous and varying regulatory requirements of such countries regarding quality, safety and efficacy. Other countries also have their own regulations governing, among other things, clinical trials and commercial sales, as well as pricing and distribution of our product candidates, and we may be required to expend significant resources to obtain regulatory approval and to comply with ongoing regulations in these jurisdictions.

The clinical and commercial success of our current and any future product candidates will depend on several factors, including the following:

- our ability to raise any additional required capital on acceptable terms, or at all;

- timely completion of our preclinical studies and clinical trials, which may be significantly slower, or cost more, than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- our ability to timely execute our ongoing clinical trials and enroll a sufficient number of patients on a timely basis to evaluate the potential of our product candidates in clinical development;
- whether we are required by the FDA or similar foreign regulatory agencies to conduct additional clinical trials or other studies beyond those planned to support approval of our product candidates;
- our ability to complete an IND, or similar foreign applications, enabling studies, and successfully submit an IND or similar foreign applications for future product candidates;
- acceptance of our proposed indications and primary endpoint assessments relating to the proposed indications of our product candidates by the FDA and similar foreign regulatory authorities;
- our ability to consistently manufacture our product candidates on a timely basis;
- our ability, and the ability of any third parties with whom we contract, to remain in good standing with regulatory agencies and develop, validate and maintain commercially viable manufacturing processes that are compliant with cGMPs or similar foreign requirements;
- our ability to demonstrate to the satisfaction of the FDA and similar foreign regulatory authorities the quality, safety, efficacy and acceptable risk-benefit profile of our product candidates;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates or future approved products, if any;
- the timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities;
- achieving and maintaining, and, where applicable, ensuring that our third-party contractors achieve and maintain, compliance with our contractual obligations and with all regulatory requirements applicable to our current or any future product candidates or approved products, if any;
- the willingness of physicians, operators of hospitals and clinics and patients to utilize or adopt our individualized cancer immunotherapy approach;
- our ability to successfully develop a commercial strategy and thereafter commercialize GRANITE, SLATE, CORAL or any future product candidates (including our partnered HIV therapeutic vaccine) in the United States and internationally, if approved for marketing, sale and distribution in such countries and territories, whether alone or in collaboration with others;
- the availability of coverage and adequate reimbursement from managed care plans, private insurers, government payors (such as Medicare and Medicaid) and other third-party payors for any of our product candidates that may be approved;
- the convenience of our treatment or dosing regimen;
- acceptance by physicians, payors and patients of the benefits, safety and efficacy of our product candidates or any future product candidates, if approved, including relative to alternative and competing treatments;
- patient demand for our current or future product candidates, if approved;
- our ability to establish and enforce intellectual property rights in and to our product candidates; and
- our ability to avoid third-party patent interference, intellectual property challenges or intellectual property infringement claims.

These factors, many of which are beyond our control, could cause us to experience significant delays or an inability to obtain regulatory approvals or commercialize our current or future product candidates. Even if regulatory approvals are obtained, we may never

be able to successfully commercialize any product candidates. Accordingly, we cannot provide assurances that we will be able to generate sufficient revenue through the sale of our product candidates or any future product candidates to continue our business or achieve profitability.

Clinical development involves a lengthy and expensive process with an uncertain outcome, and delays can occur for a variety of reasons outside of our control.

Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. We may experience delays in enrolling or completing our clinical trials. Additionally, we cannot be certain that studies or trials for our product candidates will begin on time, not require redesign, enroll an adequate number of subjects on time or be completed on schedule, if at all. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials;
- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;
- delays in obtaining regulatory authorization to commence a trial;
- reaching agreement on acceptable terms with prospective contract research organizations (CROs) and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining IRB, ethics committee and, where required, IBC approval at each trial site;
- recruiting an adequate number of suitable patients to participate in a trial, which can be impacted by external factors beyond our control, including, due to the COVID-19 or other pandemics;
- having subjects complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- addressing subject safety concerns that arise during the course of a trial;
- adding a sufficient number of clinical trial sites;
- supplying sufficient quantities of product candidates or other materials for use in preclinical studies or clinical trials; or
- accessing checkpoint inhibitors for use in combination with our product candidates in preclinical studies or clinical trials, including checkpoint inhibitors that have not been approved by the FDA for such use.

As demonstrated during the COVID-19 pandemic, a public health crisis (or other situation having lasting and widespread societal impact) can result in challenges and delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials, as well as delays in the commencement of our preclinical studies.

We may experience numerous adverse or unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or prevent us from receiving marketing approval or commercializing our product candidates, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- we may be affected by safety concerns that have a class effect; for example, if a competitor reports negative results with respect to a product candidate similar to those we are developing, such setbacks could negatively impact our own product development;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon our development programs, including our individualized cancer immunotherapy program;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;

- we or our third-party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls, or be unable to produce sufficient product supply to conduct and complete preclinical studies or clinical trials of our product candidates in a timely manner, or at all;

- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including noncompliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;

- the cost of clinical trials of our product candidates may be greater than we anticipate;

- the quality of our product candidates or other materials necessary to conduct preclinical studies or clinical trials of our product candidates may be insufficient or inadequate;

- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and

- future collaborators may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only moderately positive, or if there are safety concerns, we may:

- incur unplanned costs;

- be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all;

- obtain marketing approval in some countries and not in others;

- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;

- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;

- be subject to additional post-marketing testing requirements, which could be expensive and time consuming; or

- have the treatment removed from the market after obtaining marketing approval.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs or ethics committees of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board (DSMB), or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Further, conducting clinical trials in foreign countries, as we have done in our collaborations related to CORAL and may do for certain of our other product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, we fail to ensure such relationships and compensation are accurately disclosed, or a regulatory

authority concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of the marketing application we submit. Any such delay or rejection could prevent or delay us from commercializing our current or future product candidates.

If any of our preclinical studies or clinical trials of our product candidates are delayed or terminated, the commercial prospects of our product candidates may be harmed, and our ability to generate revenues from any of these product candidates could be delayed or not realized at all. In addition, any delays in completing our clinical trials may increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. If our product candidates or our immunotherapy prediction platform generally prove to be ineffective, unsafe or commercially unviable, our entire platform and approach would have little, if any, value, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the European Union recently evolved. The CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate CTA to be submitted in each member state to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors were still able to choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

It is currently unclear to what extent the United Kingdom, as a free-standing regulatory regime outside of the European Union, will seek to amend its regulations so that they diverge from the regulatory regime in the European Union. The UK regulatory framework in relation to clinical trials is derived from the EU Clinical Trials Directive (as implemented into UK law, through secondary legislation) in place prior to the date of application of the CTR. On January 17, 2022, the MHRA launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022 (although a response has not yet been published) and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation will be closely watched and will determine whether the United Kingdom chooses to align with the new EU CTR or diverge from it to maintain regulatory flexibility. A decision by the United Kingdom not to closely align its regulations with the CTR may have an effect on the cost of conducting clinical trials in the United Kingdom as opposed to other countries and/or make it harder to seek a marketing authorization in the European Union for our product candidates on the basis of clinical trials conducted in the United Kingdom.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may also be impacted.

Our tumor-specific cancer immunotherapy approach is based on novel ideas and technologies that are unproven and may not result in marketable products, which exposes us to unforeseen risks and makes it difficult for us to predict the time and cost of product development and potential for regulatory approval.

Regarding our tumor-specific cancer immunotherapies, our foundational science and product development approach are based on our ability to predict the presence of a patient's TSNA and develop a TSNA-directed therapy that will elicit a meaningful T cell response. We believe that this approach may offer an improved therapeutic effect by driving an intense, focused T cell attack selectively upon a patient's tumor. However, this approach to treating cancer is novel and the scientific research that forms the basis of our efforts to predict the presence of TSNA and to develop TSNA-directed cancer immunotherapy candidates is both preliminary and limited. The results of our preclinical animal studies may not translate into humans. For example, our prediction model may fail to accurately predict the presence of TSNA, resulting in little or no tumor-targeted T cell response, or our therapy may fail to elicit a significant or durable enough T cell response to effectively destroy a tumor. As such, we cannot assure you, even if we are able to develop individualized

cancer immunotherapy candidates capable of recognizing TSNA and eliciting a T cell response, that such therapy would safely and effectively treat cancers. We may spend substantial funds attempting to develop this approach and never succeed in developing a marketable therapeutic.

No regulatory authority has granted approval for a cancer immunotherapy based on a heterologous prime-boost approach, which may increase the complexity, uncertainty and length of the regulatory approval process for our product candidates. We may never receive approval to market and commercialize any product candidate. Even if we obtain regulatory approval, the approval may be for targets, disease indications, lines of therapy or patient populations that are not as broad as we intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We may be required to perform additional or unanticipated clinical trials to obtain approval or be subject to post-marketing testing requirements to maintain regulatory approval. If our personalized immunotherapy candidates prove to be ineffective, unsafe or commercially unviable, our entire technology platform and pipeline would have little, if any, value, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

The regulatory approval process and clinical trial requirements for novel product candidates can be more expensive and take longer than for other, better known or more extensively studied product candidates, and we cannot predict how long it will take or how much it will cost to complete clinical developments and obtain regulatory approvals for a cell therapy product candidate in the United States or how long it will take to commercialize a product candidate, if and when approved. Regulatory requirements governing cell therapy products have changed frequently and may continue to change in the future. For example, the FDA established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of cell therapies and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. These and other regulatory review agencies, committees and advisory groups and the requirements and 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 these treatment candidates or lead to significant post-approval limitations or restrictions. Additionally, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

Even if our product candidates obtain required regulatory approvals, such approvals may later be withdrawn as a result of changes in regulations or the interpretation of regulations by applicable regulatory agencies. Additionally, adverse developments in clinical trials conducted by others of cell therapy products or products created using similar technology, or adverse public perception of the field of cell therapies editing, may cause the FDA and other regulatory bodies to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing technologies such as ours, either of which could materially harm our business. As we advance our product candidates, we will be required to consult with various regulatory authorities, and we must comply with applicable laws, rules and regulations, which may change from time to time, including during the course of development of our product candidates. If we fail to do so, we may be required to delay or discontinue the clinical development of certain of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Even if we comply with applicable laws, rules, and regulations, and even if we maintain close coordination with the applicable regulatory authorities with oversight over our product candidates, our development programs may fail to succeed. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market would materially adversely affect our business, financial condition, results of operations and prospects.

Results of earlier studies and trials of our product candidates may not be predictive of future trial results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure or delay can occur at any time during the clinical trial process. Success in preclinical studies and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in clinical trials, even after positive results in earlier preclinical studies or clinical trials. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway and safety or efficacy observations made in clinical trials, including previously unreported adverse events. Notwithstanding any promising results we may have observed in earlier studies and trials, we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates. In addition, the results of our preclinical animal studies, including our non-human primate studies, may not be predictive of the results of outcomes in human clinical trials. For example, our tumor-specific cancer immunotherapy candidates and any future product candidates may demonstrate different chemical, biological and pharmacological properties in patients than they do in laboratory studies or may interact with human biological systems in unforeseen

or harmful ways. Product candidates in later stages of clinical trials may fail to show the desired pharmacological properties or safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. Even if we are able to initiate and complete clinical trials, the results may not be sufficient to obtain regulatory approval for our product candidates.

Our product candidates are biologics with complex and time-consuming manufacturing processes, and we may encounter difficulties in production, particularly with respect to process development or scaling-out of our manufacturing capabilities. If we or any of our third-party manufacturers encounter such difficulties, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

Our immunotherapy product candidates, GRANITE, SLATE and CORAL, are considered to be biologics, and the manufacturing processes are complex, time-consuming, highly-regulated and subject to multiple risks. Our product candidates for SLATE and CORAL are designed using known genetic sequences available from public databases, while the manufacture of our product candidate GRANITE involves extraction of genetic material from patient tumor samples. GRANITE, SLATE and CORAL require genetic manipulations at the gene sequence level, live cell culture operations, specialized formulations and aseptic fill finish operations. As a result of these complexities, the cost to manufacture biologics in general, and our individualized immunotherapy GRANITE in particular, is generally higher than traditional small molecule chemical compounds, and the manufacturing process is less reliable and more difficult and time-consuming to reproduce. In addition, our manufacturing processes for GRANITE and SLATE are in their early stages of development and will be susceptible to product loss or failure, or product variation that may adversely impact patient outcomes. Our supply chain may not function efficiently due to logistical issues associated with but not limited to the collection of a tumor biopsy from the patient, shipping such material to the manufacturing site, sequencing the biopsy specimen, manufacturing the immunotherapy components, shipping the final immunotherapy back to the patient, and injecting the patient with the immunotherapy. Manufacturing issues or different product characteristics resulting from process development activities or even minor deviations during normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If for any reason we lose a patient's biopsy or an in-process product at any point in the process, the manufacturing process for that patient would need to be restarted, and the resulting delay could adversely affect that patient's outcome. Because GRANITE is manufactured specifically for an individual patient, we will be required to maintain a chain of identity and chain of custody with respect to materials as they move from the patient to the manufacturing facility, through the manufacturing process, and back to the patient. Maintaining such a chain of identity and chain of custody is difficult and complex, and the failure to do so could result in adverse patient outcomes, loss of product or regulatory action, including withdrawal of our products from the market, if licensed.

As part of our process development efforts for GRANITE and SLATE, we also may make changes to our manufacturing processes at various points during development, for various reasons, such as controlling costs, achieving scale, decreasing processing time, increasing manufacturing success rate, or other reasons. Such changes carry the risk that they will not achieve their intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of our ongoing clinical trials or future clinical trials. In some circumstances, changes in the manufacturing process may require us to perform ex vivo comparability studies and to collect additional data from patients prior to undertaking more advanced clinical trials. For instance, changes in our process during the course of clinical development may require us to show the comparability of the product used in earlier clinical phases or at earlier portions of a trial to the product used in later clinical phases or later portions of the trial.

Furthermore, if microbial, viral or other contaminations are discovered in our manufacturing facilities, or those of our CMOs, or in our product candidates manufactured there, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any such contaminations or stability failures or other issues relating to the manufacture of our product candidates will not occur in the future.

We may be unable to obtain regulatory approval for our product candidates under applicable regulatory requirements. The denial or delay of any such approval would delay or prevent commercialization of our product candidates and adversely impact our potential to generate revenue, our business and our results of operations.

To gain approval to market our product candidates, we must provide the FDA and foreign regulatory authorities with clinical data that adequately demonstrate the safety, purity, potency and efficacy of the product candidate for the intended indication applied for in the applicable regulatory filing. Product development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our clinical development programs. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in clinical trials, even after promising results in earlier preclinical or clinical trials. These setbacks have been caused by, among other things, preclinical findings made while clinical studies were underway and safety or efficacy observations made in clinical trials, including previously unreported adverse events. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and the results of clinical trials by other parties may not be indicative of the results in trials we may conduct.

We have not previously submitted a BLA or any other marketing application to the FDA or similar filings to comparable foreign regulatory authorities. A BLA or other similar regulatory filing requesting approval to market a product candidate must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe, effective, pure and potent for each desired indication. The BLA or other similar regulatory filing must also include significant information regarding the chemistry, manufacturing and controls for the product. FDA and foreign regulatory authorities may also conduct pre-license inspections of us and/or our CMOs to ensure the manufacture of a product candidate complies with applicable regulatory requirements, including cGMP or similar foreign requirements. Adverse inspection findings could result in the delay or non-approval of a BLA or other similar regulatory filing and require the implementation of costly corrective actions before potential approval can be granted.

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of biologic products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, and such regulations differ from country to country. We are not permitted to market our product candidates in the United States or in any foreign countries until they receive the requisite approval from the applicable regulatory authorities of such jurisdictions.

The FDA or any foreign regulatory bodies can delay, limit or deny approval of our product candidates for many reasons, including:

- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory body that any of our product candidates are safe, pure, potent and effective for the requested indication;
- the FDA's or the applicable foreign regulatory agency's disagreement with our trial protocols or the interpretation or reliability of data from preclinical studies or clinical trials;
- our inability to demonstrate that the clinical and other benefits of any of our product candidates outweigh any safety or other perceived risks;
- the FDA's or the applicable foreign regulatory agency's requirement for additional preclinical studies or clinical trials;
- the FDA's or the applicable foreign regulatory agency's non-approval of the formulation, labeling or specifications of GRANITE, SLATE, or any of our other current or future product candidates;
- the FDA's or the applicable foreign regulatory agency's failure to approve our manufacturing processes and facilities or the facilities of third-party manufacturers upon which we rely; or
- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval. For example, the FDA launched Project Optimus as an initiative to reform the dose optimization and dose selection paradigm in oncology product development as the FDA's view is that the current paradigm for dose selection results in doses and schedules of molecularly targeted therapies that are inadequately characterized before initiating registration/pivotal trials. Through collaboration with industry, academia, and other stakeholders, the FDA's goal for this initiative is to advance an oncology dose-finding and dose optimization paradigm that emphasizes dose selections that maximize efficacy as well as safety and tolerability. In support of this initiative, the FDA may request sponsors of oncology product candidates to conduct dose optimization studies pre- or post-approval. The FDA also continues to develop and finalize guidance documents and implement initiatives regarding the development and clinical research of oncology product candidates.

Additionally, in part due to questions raised by the process underlying the approval of the Alzheimer's disease drug Aduhelm®, government authorities and other stakeholders have been recently scrutinizing the accelerated approval pathway, with some stakeholders advocating for reforms. Even prior to the Aduhelm approval, FDA has held Oncologic Drugs Advisory Committee meetings to discuss accelerated approvals for which confirmatory trials have not verified clinical benefit. Such scrutiny, among other factors, has resulted in voluntary withdrawals of certain products and indications approved on an accelerated basis. FDA also launched an initiative, known as Project Confirm, to promote the transparency of outcomes related to accelerated approvals for oncology indications. Moreover, spurred by the Aduhelm controversy, the U.S. Department of Health and Human Services Office of Inspector General has initiated, and partially completed, an assessment of how the FDA implements the accelerated approval pathway. In addition, Section 3210 of the Consolidated Appropriations Act, 2023, revised the accelerated approval pathway. Although this legislation did not change the standard for accelerated approval, it, among other things, requires FDA to specify the conditions for required post-marketing trials, permits FDA to require such trials to be underway prior to, or within a specific period after, approval, requires sponsors to provide reports on post-marketing trial progress no later than 180 days after approval and every 180 days thereafter until such trials are completed, makes the failure to conduct required post-marketing trials with due diligence and the failure to submit the required reports prohibited acts, and

details procedures FDA must follow to withdraw an accelerated approval on an expedited basis. At this time, it is not clear what, if any, impact these developments may have on the statutory accelerated approval pathway or our business, financial condition, results of operations or prospects.

Of the large number of biopharmaceutical products in development, only a small percentage successfully complete the FDA or other regulatory bodies' approval processes and are commercialized.

Even if we eventually complete clinical testing and receive approval from the FDA or applicable foreign agencies for any of our product candidates, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials which may be required after approval. Failure to complete such post-marketing requirements in accordance with the timelines and conditions set forth by the FDA or the applicable foreign regulatory agency could significantly increase costs or delay, limit or ultimately restrict the commercialization of the product candidate. The FDA or the applicable foreign regulatory agency also may approve one or more of our product candidates for a more limited indication or a narrower patient population than we originally requested, and the FDA, or applicable foreign regulatory agency, may not approve our product candidates with the labeling that we believe is necessary or desirable for the successful commercialization of such product candidates.

Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of our product candidates and would materially adversely impact our business and prospects.

We have chosen to prioritize development of our individualized immunotherapy candidate, GRANITE, and our off-the-shelf immunotherapy candidate, SLATE. We may expend our limited resources on candidates or indications that do not yield a successful product and fail to capitalize on other product candidates or indications for which there may be a greater likelihood of success or that may be more profitable.

In our cancer programs, we strategically determined initially to focus solely on the development of individualized cancer immunotherapy candidates (including our "off-the-shelf" immunotherapy candidate) rather than pursue other types of immunotherapies based, in part, on the significant resources required to develop and manufacture immunotherapies. As a result, we may initially have foregone, and we may continue to forego, other potentially more profitable therapy indications or those with a greater likelihood of success.

Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties in respect of certain programs may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the oncology or biopharmaceutical industry, our business, financial condition and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain development and commercialization rights.

If we are unable to obtain regulatory approval for use of our tumor-specific immunotherapy candidates, GRANITE and SLATE, as a first- and second-line therapy, our commercial opportunity and profitability may be limited.

Cancer therapies for advanced/metastatic cancers are sometimes characterized as first-line, second-line or third-line, and the FDA often approves new systemic therapies initially only for third-line use. When cancer is detected early enough, surgery plus first-line systemic therapy is sometimes adequate to cure the cancer. Whenever first-line therapy (usually chemotherapy, hormone therapy, radiotherapy, surgery or a combination of these) proves unsuccessful, second-line therapy may be administered. Second-line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules or a combination of these. Third-line therapies can include bone marrow transplantation, antibody and small molecule targeted therapies and new technologies such as adoptive cell therapies.

Traditionally, novel oncology therapeutics are developed and approved in late (third) line therapy of cancer patients. Such clinical programs carry risk of failure because patients are often quite frail, with effects of multiple rounds of prior therapy weakening bone marrow, immune systems and general fitness. Immunotherapy, such as checkpoint inhibitors, has generally been shown to be more effective when used in earlier lines of therapy, with the prospect of very durable responses in some patients; and there is a trend towards earlier use of these agents, avoiding in particular cytotoxic chemotherapy agents, which carry substantial toxicity and very little prospect of long-term responses. Our tumor-specific immunotherapy clinical development program also aims to study our products in early stages

of cancer treatment (referred to as adjuvant therapy), which carry a higher safety bar, and often a greater expectation of efficacy over control arms. Such studies may thus be relatively large and slow to achieve maturity. There are new tools available to stratify cancer patients for risk of recurrence or progression, such as liquid biopsies that measure the amount of circulating tumor-derived DNA. We will utilize these tools to attempt to expedite clinical trials in early-stage cancer patients by focusing upon patients at above-average risk of disease recurrence or progression, which events are typical endpoints in clinical trials. The development of liquid biopsies is at an early stage, however, and these tools may prove to carry low utility and thus render early-stage cancer trials slow, necessarily large and expensive. The safety of our tumor-specific immunotherapy product candidates in combination with checkpoint inhibitors in early lines of therapy may also prove to be unacceptable.

We expect to seek approval of our tumor-specific immunotherapy product candidates as a first-line therapy wherever possible, but also as a late-line therapy where appropriate, and potentially as adjuvant therapy. There is no guarantee that our product candidates, even if approved in late-line therapy, would be approved for second-line or first-line or adjuvant therapy. In addition, we may have to conduct additional clinical trials prior to gaining approval for first-line or adjuvant therapy.

While our SLATE product is designed to be readily available (off-the-shelf), GRANITE may initially take approximately 14 to 18 weeks post-sequencing to be manufactured and released for human use, and this long timeline demands that either patients are consented and entered into our trials when they start a prior line of therapy, and start our therapy upon disease progression, or we initiate treatment in patients who have entered the maintenance phase of their original line of treatment. For example, we might enroll newly diagnosed patients who are due to receive front-line chemotherapy and then start their therapy with our immunotherapy product candidate as second-line treatment when they progress upon front-line chemotherapy or fail to tolerate it. This carries the risk of time delays or drop-out, i.e., patients may not progress after first-line chemotherapy for a long time, or they may decide not to receive an immunotherapy product candidate we have manufactured for them, at our expense. Alternatively, we may treat first-line patients once they have completed their initial treatment and have not progressed (called maintenance therapy)—this renders efficacy harder to interpret versus simple treatment studies (any objective response cannot clearly be attributed to our products) and may be complicated by standard of care treatments, which may necessarily be continued alongside our immunotherapy candidates, further confounding interpretation of efficacy.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive first-, second- or third-line therapy and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations, and market research, and may prove to be incorrect. Regulatory authorities also may establish narrower definitions around when a patient is ineligible for other treatments than we have used in our projections, and that would reduce the size of the patient population eligible for our product candidates. Further, new studies may change the estimated incidence or prevalence of these cancers. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates. For instance, we anticipate that only a fraction of colorectal cancer patients will be predicted to have a high enough probability of TSNA presence to merit their inclusion into our program. Even if we obtain significant market share for our product candidates, because the potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications, including use as a first-line or second-line therapy.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

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

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial’s primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinical trial investigators’ willingness to enroll patients during a public health crisis, such as the COVID-19 pandemic;

- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new therapies that may be approved for the indications we are investigating; and

- our ability to obtain and maintain patient consents.

Our clinical trials may compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and such competition may reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. In addition, as we have faced challenges with patient enrollment and monitoring once on study due to the COVID-19 pandemic, similar challenges are likely in case of a resurgence of the COVID-19 pandemic or if another such public health crisis were to occur.

Further, the targeting of TSNA may result in unforeseen events, including harming healthy tissues in humans. As a result, it is possible that safety concerns could negatively affect patient enrollment among the patient populations that we intend to treat. Delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

As with most biological products, use of our product candidates could be associated with side effects or adverse events, which can vary in severity from minor reactions to death and in frequency from infrequent to prevalent. Undesirable side effects or unacceptable toxicities caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. While we have now completed the Phase 1 portions, and we are in the Phase 2 portions, of our clinical trials of GRANITE and SLATE, we do not yet have a comprehensive understanding of their risks, and it is likely that there will be side effects associated with their use in increasing numbers of patients in Phase 2 and beyond. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. Our other product candidates present similar risks, the severity of which is difficult to predict.

If unacceptable side effects arise in the development of our product candidates, we, the FDA, or comparable foreign regulatory authorities, the IRBs at the institutions in which our studies are conducted, or the DSMB could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete any of our clinical trials or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition, even if we successfully advance one of our product candidates through clinical trials, such trials will likely only include a limited number of subjects and limited duration of exposure to our product candidates. As a result, we cannot be assured that adverse effects of our product candidates will not be uncovered when a significantly larger number of patients are exposed to the product candidate. Further, any clinical trials may not be sufficient to determine the effect and safety consequences of taking our product candidates over a multi-year period.

There have been several reported cases of severe thrombosis with thrombocytopenia occurring post-vaccination in individuals who received adenovirus-based vaccines for SARS-CoV-2, including those administered under EUA. This syndrome has been termed "vaccine-induced prothrombotic immune thrombocytopenia (VIPIT)" or "vaccine-induced immune thrombotic thrombocytopenia (VITT)" but is now termed "thrombosis with thrombocytopenia syndrome (TTS)" by the Centers for Disease Control and Prevention (CDC) and the FDA. The syndrome appears to be autoimmune in nature and is associated with autoantibodies to a specific platelet-associated antigen. To date, no patients receiving our adenoviral vaccine candidate against SARS-CoV-2, CORAL, have been known to develop TTS, nor have we observed it in our cancer programs where our adenoviral vaccines are used in conjunction with checkpoint inhibitors (e.g., anti-PD1 antibody), which themselves can be associated with autoimmune toxicities; but we cannot be certain that this or similar complications will not arise.

If any of our product candidates receives marketing approval and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may vary, suspend or revoke their approval of the product;

- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we may be required to implement a Risk Evaluation and Mitigation Strategy (REMS), or similar risk management measures, or create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenues to us, which would materially adversely affect our results of operations and business. In addition, if one or more of our product candidates or our TSNA-directed immunotherapy approach generally prove to be unsafe, our entire technology platform and pipeline could be affected, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

Even if one of our product candidates obtains regulatory approval, it may fail to achieve the broad degree of physician and patient adoption and use necessary for commercial success.

Even if one of our product candidates receives FDA or other regulatory approvals, the commercial success of any of our current or future product candidates will depend significantly on the broad adoption and use of the resulting product by physicians and patients for approved indications. The degree and rate of physician and patient adoption of our current or future product candidates, if approved, will depend on a number of factors, including:

- the clinical indications for which the product is approved and patient demand for approved products that treat those indications;
- the safety and efficacy of our product as compared to other available therapies;
- the time required for manufacture and release of our individualized immunotherapy products;
- the availability of coverage and adequate reimbursement from managed care plans, private insurers, government payors (such as Medicare and Medicaid) and other third-party payors for any of our product candidates that may be approved;
- acceptance by physicians, operators of hospitals and clinics and patients of the product as a safe and effective treatment;
- physician and patient willingness to adopt a new therapy for appropriate patients versus other available therapies for a particular indication;
- proper training and administration of our product candidates by physicians and medical staff;
- patient satisfaction with the results and administration of our product candidates and overall treatment experience, including, for example, the convenience of any dosing regimen;
- the cost of treatment with our product candidates in relation to alternative treatments and reimbursement levels, if any, and willingness to pay for the product, if approved, on the part of insurance companies and other third-party payers, physicians and patients;
- the prevalence and severity of side effects;
- limitations or warnings contained in the FDA or foreign regulatory authorities - approved labeling for our products;

- the willingness of physicians, operators of hospitals and clinics and patients to utilize or adopt our products as a solution;
- any FDA or foreign regulatory authorities' requirement for a REMS or similar risk management measures;
- the effectiveness of our sales, marketing and distribution efforts;
- adverse publicity about our products or favorable publicity about competitive products; and
- potential product liability claims.

We cannot assure you that our current or future product candidates, if approved, will achieve broad market acceptance among physicians and patients. Any failure by our product candidates that obtain regulatory approval to achieve market acceptance or commercial success would adversely affect our results of operations.

We currently perform most of the manufacturing of our product candidates internally and rely on qualified third parties to supply some components of our product candidates. Our inability to manufacture sufficient quantities of any of our current or future product candidates, or the loss of our third-party suppliers, or our or their failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, would materially adversely affect our business.

Manufacturing is a vital component of our immunotherapy approach, and we have invested significantly in our manufacturing facility. To ensure timely and consistent product supply assurance to our patients, we previously used a hybrid product supply approach whereby certain elements of our product candidates were manufactured internally at our manufacturing facilities in Pleasanton, California, and other elements were manufactured at qualified third-party contract manufacturing organizations (CMOs). All internal and third-party contract manufacturing is performed under cGMP or similar guidelines. We have since internalized most of the manufacturing steps to optimize cost and production time and establish full control over intellectual property and product quality. We will need to continue to scale up our manufacturing operations, as we continue to build the infrastructure and improve the capability internally to manufacture all supplies needed for our product candidates or the materials necessary to produce them for use in the conduct of our preclinical studies or clinical trials. We currently lack the internal resources and the capability to manufacture certain elements of our product candidates on a late-clinical or commercial scale. Accordingly, we have made, and will be required to continue to make, significant investments in our manufacturing facility and processing in the future, and our efforts to scale our manufacturing operations may not succeed.

Our facilities and the facilities used by our CMOs to manufacture our product candidates are subject to various regulatory requirements and may be subject to inspection by the FDA or other regulatory authorities. We do not control the manufacturing process at our CMOs and are completely dependent on them for compliance with current regulatory requirements. If we or our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or comparable regulatory authorities in foreign jurisdictions, we may not be able to rely on our or their manufacturing facilities for the manufacture of elements of our product candidates. In addition, we have limited control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority finds our facilities or those of our CMOs inadequate for the manufacture of our product candidates, or if such facilities are subject to enforcement action in the future or are otherwise inadequate, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates.

Additionally, even if one of our product candidates receives regulatory approval, successful commercialization depends on our ability to effectively scale up our in-house manufacturing capabilities and those of our manufacturing partners and contractors. Although we have a dedicated manufacturing facility in Pleasanton, we do not have sufficient manufacturing infrastructure to support a global roll-out of our product candidates on our own. We may not be able to timely and effectively produce our product candidates, if approved, in adequate quantities to address global demand. We have not previously had a commercial launch of any product, and we cannot guarantee that we will be able to meet any of the related challenges and requirements in a timely manner or at all.

Finally, we and our CMOs may experience manufacturing and raw material sourcing difficulties due to resource constraints, as a result of labor disputes or unstable political environments, or due to the impact of a public health crisis such as the COVID-19 pandemic. If we or our CMOs were to encounter any of these difficulties, our ability to provide our product candidates to patients in clinical trials, or to provide product for the treatment of patients once approved, would be jeopardized.

We depend on third-party suppliers for key materials used in our manufacturing processes, and the loss of these third-party suppliers or their inability to supply us with adequate materials could harm our business.

We rely on third-party suppliers for certain materials required for the production of our individualized immunotherapy candidate. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of materials involve several risks, including limited control over pricing, availability, quality and delivery schedules. As a small company, our negotiation leverage is limited, and we are likely to get lower priority than our larger competitors. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

We rely, and intend to continue to rely, on third parties in the conduct of all of our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, fail to comply with applicable regulatory requirements or fail to meet expected deadlines, we may be unable to obtain regulatory approval for our product candidates.

We currently do not have the ability to independently conduct preclinical studies that comply with good laboratory practice (GLP) regulatory requirements. We also do not currently have the ability to independently conduct any clinical trials. The FDA and regulatory authorities in other jurisdictions require us to comply with regulations and standards, commonly referred to as good clinical practice (GCP) requirements for conducting, monitoring, recording and reporting the results of clinical trials, in order to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct GLP-compliant preclinical studies and GCP-compliant clinical trials on our product candidates properly and on time. While we have agreements governing their activities, we control only certain aspects of their activities and have limited influence over their actual performance. The third parties with whom we contract for execution of our GLP-compliant preclinical studies and our GCP-compliant clinical trials play a significant role in the conduct of these studies and trials and the subsequent collection and analysis of data. These third parties are not our employees and, except for restrictions imposed by our contracts with such third parties, we have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely on these third parties to conduct our GLP-compliant preclinical studies and GCP-compliant clinical trials, we remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities.

Many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. Further, under certain circumstances, these third parties may terminate their agreements with us upon as little as 10 days' prior written notice. Some of these agreements may also be terminated with immediate effect by such third parties under certain other circumstances, including our insolvency. If the third parties conducting our preclinical studies or our clinical trials do not adequately perform their contractual duties or obligations, experience significant business challenges, disruptions or failures, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to our protocols or to GLPs/GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties. This could be difficult, costly or impossible, and our preclinical studies or clinical trials may need to be extended, delayed, terminated or repeated. As a result, we may not be able to obtain regulatory approval in a timely fashion, or at all, for the applicable product candidate, our financial results and the commercial prospects for our product candidates could be harmed, our costs could increase, and our ability to generate revenues could be delayed.

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 or foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory and policy changes, the FDA's or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities 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 approved biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the

U.S. government has shut down several times, and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA utilized this risk-based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plan to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities. According to the guidance, the FDA may request such remote interactive evaluations where the FDA determines that remote evaluation would be appropriate based on mission needs and travel limitations. In May 2021, the FDA outlined a detailed plan to move toward a more consistent state of inspectional operations, and in July 2021, the FDA resumed standard inspectional operations of domestic facilities and was continuing to maintain this level of operation as of September 2021. More recently, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic and has also indicated that it intends to utilize remote regulatory assessments and other alternative tools beyond the COVID-19 pandemic. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We face significant competition in an environment of rapid technological and scientific change, and our failure to effectively compete may prevent us from achieving significant market penetration. Most of our competitors have significantly greater resources than we do, and we may not be able to successfully compete.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on developing proprietary therapeutics. We compete with a variety of multinational biopharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions. Our competitors have developed, are developing or will develop product candidates and processes that may compete with our product candidates. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments that enter the market. We believe that a significant number of product candidates are currently under development, and may become commercially available in the future, for the treatment of diseases and other conditions for which we may try to develop product candidates. There is intense and rapidly evolving competition in the biotechnology, biopharmaceutical and antibody and immunoregulatory therapeutics fields. We believe that, while our discovery platform, its associated intellectual property and our scientific and technical know-how give us a competitive advantage in this space, competition from many sources remains. Our competitors include larger and better funded biopharmaceutical, biotechnological and therapeutics companies. Moreover, we also compete with current and future therapeutics developed at universities and other research institutions.

Our success will partially depend on our ability to develop and protect therapeutics that are safer and more effective than competing products. Our commercial opportunity and success will be reduced or eliminated if competing products that are safer, more effective, or less expensive than the therapeutics we develop.

For example, if either of our GRANITE or SLATE vaccine candidates is approved, it will compete with a range of therapeutic treatments that are either in development or currently marketed, of which there are many. Such marketed therapies range from immune checkpoint inhibitors such as Bristol-Myers Squibb Company’s OPDIVO and YERVOY, Merck & Co., Inc.’s KEYTRUDA, AstraZeneca’s IMFINZI, and Genentech, Inc.’s TECENTRIQ, T cell engager immunotherapies such as Amgen, Inc.’s BLINCYTO, and multi-kinase inhibitors such as Bayer’s STIVARGA. The most common therapeutic treatments for common solid tumors are chemotherapeutic compounds, radiation therapy, targeted therapies and now immunotherapies. In addition, numerous compounds are in clinical development for cancer treatment. The clinical development pipeline for cancer treatments includes small molecules, antibodies and immunotherapies from a variety of groups, including in the neoantigen space, the bispecific antibody space and engineered cell therapy and T cell receptor (TCR) space. Many of these companies are well-capitalized and, in contrast to us, have significant clinical experience.

Despite funding provided to us to date, many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage

and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. If any competitors are successful in producing more efficacious products or if any competitors are able to manufacture and distribute competitive products with greater efficiency there may be a diversion of potential governmental and other funding away from us and toward such other parties. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

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

The availability of coverage and adequacy of reimbursement by managed care plans, governmental healthcare programs, such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates that receive FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement for our products or procedures using our products by third-party payors will have an effect on our ability to successfully commercialize our product candidates. Obtaining coverage and adequate reimbursement for our products may be particularly difficult due to general price sensitivity associated with drugs administered under the supervision of a physician. Separate reimbursement for the product itself or the treatment or procedure in which our product is used may not be available. A decision by a third-party payor not to cover or separately reimburse for our products, or procedures using our products, could reduce physician utilization of our products once approved. Assuming there is coverage for our product candidates, or procedures using our product candidates, by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the European Union Member States or elsewhere will be available for our product candidates or procedures using our product candidates, or any product that we may develop, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may not necessarily inform the price for our product candidates. These third-party payors may deny or revoke the reimbursement status of our product candidates, if approved. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly-approved products, especially novel products like our immunotherapy product candidates. No regulatory authority has granted approval for a tumor-specific cancer immunotherapy based on a vaccine approach, and there is no model for reimbursement of this type of product. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that may require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that future changes in these rules and regulations are likely. In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could

restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products, and, as a result, they may not cover or provide adequate payment for our product candidates. For example, the recently-enacted Inflation Reduction Act directs the Secretary to negotiate maximum fair prices for certain Medicare drugs. The law also requires manufacturers to pay a rebate if the price of a Medicare Part B or Part D drug increases at a rate that exceeds inflation and redesigns the Medicare Part D benefit in a way that potentially obligates manufacturers to increased discounts on Part D utilization. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

If we are unable to support demand for our existing or future services, including ensuring that we have adequate capacity to meet increased demand, or we are unable to successfully manage the evolution of our EDGE™ platform, our business could suffer.

As the demand for our individualized and off-the-shelf vaccine-based immunotherapy candidates increases with our clinical trial needs, we will need to continue to increase our workflow capacity for sample intake and general process improvements, expand our internal quality assurance program, and apply our EDGE™ platform at a larger scale within expected turnaround times. We will need additional certified laboratory scientists and technicians and other scientific and technical personnel to process higher volumes of tumor biopsies. Portions of our process are not automated and will require additional personnel to scale. We will also need to purchase additional equipment, some of which can take several months or more to procure, set up, and validate, and increase our software and computing capacity to meet increased volume. There is no assurance that any of these increases in scale, expansion of personnel, equipment, software and computing capacities, or process enhancements will be successfully implemented, or that we will have adequate space in our laboratory facilities to accommodate such required expansion.

As we progress into clinical development and expand our manufacturing capabilities, we will need to incorporate new equipment, implement new technology systems and laboratory processes, and hire new personnel with different qualifications. Failure to manage this growth or transition could result in turnaround time delays, higher service costs, declining service quality, deteriorating customer service, and slower responses to competitive challenges. A failure in any one of these areas could make it difficult for us to meet market expectations for our services and could damage our reputation and the prospects for our business.

We currently have no sales organization. If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell our product candidates effectively in the United States and foreign jurisdictions, if approved, or generate product revenue.

We currently do not have a marketing or sales organization. In order to commercialize our product candidates, if approved, in the United States and foreign jurisdictions, we will need to build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If any of our product candidates receive regulatory approval, we expect to establish a sales organization with technical expertise and supporting distribution capabilities to commercialize each such product candidate, which will be expensive and time consuming. We have no prior experience in the marketing, sale and distribution of pharmaceutical products, and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain, and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of them. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our product candidates. If we are not successful in commercializing our current or any future product candidates, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

We will need to increase the size of our organization, and we may experience difficulties in managing growth.

As of December 31, 2022, we had 233 full-time employees. As our clinical trials progress and we get closer to any potential regulatory approvals, we will need to expand our managerial, regulatory, clinical science, development operations, finance and other resources in order to manage our operations and clinical trials, continue our development activities and commercialize our product

candidates or any future product candidates. Our management and personnel, systems and facilities currently in place may not be adequate to support our future needs. Our need to effectively execute on our growth strategy requires that we:

- manage our preclinical studies and clinical trials effectively;
- identify, recruit, retain, incentivize and integrate additional employees, including sales personnel;
- manage our internal development and operational efforts effectively while carrying out our contractual obligations to third parties; and
- continue to improve our operational, financial and management controls, reports systems and procedures.

If we fail to attract and retain senior management and key scientific personnel, our business may be materially adversely affected.

Our success depends in part on our continued ability to attract, retain and motivate highly-qualified management, clinical and scientific personnel. We are highly dependent upon our senior management, particularly our President and Chief Executive Officer, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals could delay or prevent the successful development of our products, initiation or completion of our planned clinical trials or the commercialization of our current or any future product candidates.

Competition for qualified personnel in the biotechnology and biopharmaceutical fields is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and if we initiate commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all. In addition, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our current or future product candidates.

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

- decreased demand for our current or future product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management’s time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize our current or any future product candidates.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of our current or any future product candidates we develop. We currently carry product liability insurance covering our clinical trials in the amount of $10.0 million in the aggregate. Nonetheless, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient funds to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. If and when we obtain approval for marketing any of our product candidates, we intend to expand our insurance coverage to include the sale of such product candidate; however, we may be unable to obtain this liability insurance on commercially reasonable terms or at all.

Our strategic collaborations, including those with Gilead and with 2seventy as well as any future arrangements that we may enter into, may not be successful, which could significantly limit the likelihood of receiving the potential economic benefits of such collaborations and adversely affect our ability to develop and commercialize our product candidates.

In February 2021, we announced that we had entered into a collaboration, option and license agreement with Gilead to research and develop a vaccine for HIV. Under the terms of the agreement, Gilead is responsible for conducting the Phase 1 study and, if it exercises its exclusive option, will develop and commercialize the HIV-specific therapeutic vaccine beyond Phase 1. In such case, subject to certain clinical, regulatory and commercial milestones being achieved, we would be eligible to receive up to an additional $725.0 million, as well as certain royalties on net sales upon commercialization. Separately, in August 2018, we entered into a strategic collaboration with 2seventy to utilize our EDGE™ platform to identify and validate tumor-specific targets and provide TCRs directed to 10 selected targets for use in 2seventy's cell therapy products. Under that collaboration, we are entitled to receive up to an aggregate of $1.2 billion in development, regulatory and commercial milestones and tiered single digit royalties on sales of 2seventy's cell therapy products utilizing the TCRs we develop directed at the targets we discovered.

Apart from these strategic collaborations, in the future, we may seek to enter into additional collaboration arrangements for the development or commercialization of certain of our product candidates, depending on the merits of retaining commercialization rights for ourselves as compared to entering into collaboration arrangements. To the extent that we decide to enter into collaboration agreements in the future, we may face significant competition in seeking appropriate collaborators. Moreover, all such collaboration arrangements are complex and time-consuming to negotiate, document, implement and maintain, as well as challenging to manage. We may not be successful in our efforts with Gilead or 2seventy, and we may never receive any of the payments contemplated in those collaboration arrangements. Further, we may be unable to prudently manage these collaborations or enter into new ones. The terms of any new collaborations or other arrangements that we may establish may not be favorable to us.

The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include risks that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to their acquisition of competitive products or their internal development of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;

- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;

- disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our current or future product candidates or that results in costly litigation or arbitration that diverts management attention and resources;

- collaborations may be terminated, and, if terminated, this may result in a need for additional capital to pursue further development or commercialization of the applicable current or future product candidates;

- collaborators may own or co-own intellectual property covering products that result from our collaboration with them, and, in such cases, we would not have the exclusive right to develop or commercialize such intellectual property;

- disputes may arise with respect to the ownership of any intellectual property developed pursuant to our collaborations; and

- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

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

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

- increased operating expenses and cash requirements;

- the assumption of additional indebtedness or contingent liabilities;

- the issuance of our equity securities;

- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;

- the diversion of our management's attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;

- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;

- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and

- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

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

We, or the third parties upon whom we depend, may be adversely affected by risks beyond our control, such as natural disasters, political crises, acts of terrorism, war or other catastrophic events and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

We, our suppliers and third-party service providers are vulnerable to damage from natural disasters, including but not limited to earthquakes, fires or floods, power loss, communications failures, public health crises, such as pandemics and epidemics, political

crises, such as terrorism, war, political instability or other conflict and similar events. If any disaster were to occur, our ability to operate our business at any of our facilities could be seriously, or potentially completely, impaired.

Our corporate headquarters and certain of our other facilities, including our manufacturing facility, are located in the San Francisco Bay Area, which in the past has experienced both severe earthquakes and wildfires. We do not carry earthquake insurance. Earthquakes, wildfires or other natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. For example, if a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters or other facilities, that damaged critical infrastructure, such as our enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time.

In addition, in late February 2022, Russian military forces launched significant military action against Ukraine. In response, many countries and organizations implemented new, stricter sanctions against officials, individuals, regions, and industries in Russia and Belarus. These and other actions related to Russia's invasion of Ukraine have also been a major contributing factor to high inflation as well as putting significant downward pressure on economic growth. Apart from the tragic loss of life and human suffering, the war in Ukraine has had, and likely will continue to have, an adverse effect on the global economy and political situation.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters or other facilities, that damaged critical infrastructure, such as our enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time.

The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain are similarly vulnerable to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

We depend on our information technology systems, and any failure of these systems could harm our business. Security breaches, loss of data, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability, which could adversely affect our business, results of operations and financial condition.

We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business, including our laboratory information management system and our EDGE™ platform. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We have established physical, electronic and organizational measures to safeguard and secure our systems to prevent a data compromise, and rely on commercially available systems, software, tools, and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our confidential information. Our internal information technology systems and infrastructure, and those of our current and any future collaborators, contractors and consultants and other third parties on which we rely, are vulnerable to attack and damage from computer viruses, and malware (e.g., ransomware), natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization.

The risk of a security breach or disruption or data loss, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments and cyber-terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property. We may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, either full-time or on a hybrid basis, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and

techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. We have experienced phishing attacks in the past resulting in a security breach of our information technology systems, and we may be a target of phishing attacks or other cyber-attacks in the future. Any significant system failure, accident or security breach could have a material adverse effect on our business, financial condition and results of operations. The costs to us to mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Moreover, if a computer security breach affects our systems or results in the unauthorized release of personally identifiable information, our reputation could be materially damaged. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal and state privacy and security laws, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws. We would also be exposed to a risk of loss or litigation and potential liability, which could materially adversely affect our business, results of operations and financial condition. Further, our insurance coverage may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

Our business is subject to complex and evolving laws and regulations regarding privacy, data protection and other matters relating to information collection.

There are numerous state, federal and non-U.S. laws, regulations, decisions, and directives regarding privacy and the collection, storage, transmission, use, processing, disclosure and protection of different types of personal data and personal information and other personal, customer, or other data, the scope of which is continually evolving and subject to differing interpretations. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

In the United States, although we currently are not subject to the privacy or security regulations implementing HIPAA, many of the persons and organizations with which we interact are subject to those regulations and we have to expend resources to understand their obligations, adjust contractual relationships in light of those obligations, or otherwise modify our business practices. Congress has considered expanding the scope of the HIPAA privacy and security regulations and we may in the future ourselves become subject to them or similar regulations, which would require us to make additional expenditures and create additional liability risks.

At the state level, many U.S. states in which we operate have laws that protect the privacy and security of personal information, and other states have proposed privacy legislation that may more stringent or broader in scope, or offer greater individual rights, than the laws to which we currently are subject. This patchwork of evolving privacy law complicates our compliance efforts, at considerable cost. Even a single state's privacy regime can be very complicated. For example, the California Confidentiality of Medical Information Act (the "CMIA") imposes on pharmaceutical companies strict data privacy and security requirements and obligations with respect to the personal health information of California residents and authorizes administrative fines and civil penalties of up to $25,000 for willful violations and up to $250,000 if the violation is for purposes of financial gain, as well as criminal fines. In parallel, the California Consumer Privacy Act of 2018 (the "CCPA"), which was substantially amended in 2020 pursuant to the California Privacy Rights Act (the "CPRA"), which generally went into effect on January 1, 2023, generally requires us to provide notice to California residents regarding the personal information we collect, use and share and to honor such residents' privacy rights, including the right to opt out of the sale of their personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data security breaches that result in the compromise of sensitive personal information. California's aggressive steps to protect consumer privacy have been followed by similar actions in other states, including Virginia, Colorado, Utah and Connecticut, all of which have enacted CCPA/CPRA-like laws to provide their respective residents with similar rights, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The effects on our business of this rapidly growing body of privacy and data protection laws are potentially significant, and may require us to modify our data processing practices and policies and to incur substantial costs and expenses in an effort to comply.

In the European Union, the General Data Protection Regulation (GDPR) went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the EEA. The GDPR has increased our obligations, for example, by

imposing higher standards when obtaining consent from individuals to process their personal data, requiring more robust disclosures to individuals, strengthening individual data rights, shortening timelines for data breach notifications, limiting retention periods and secondary use of information, increasing requirements pertaining to health data as well as pseudonymized (i.e., key-coded) data, and imposing additional obligations when we contract third-party processors in connection with the processing of personal data. The GDPR also regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data; in July 2020, the Court of Justice of the European Union ("CJEU") limited how organizations could lawfully transfer personal data from the EU/EEA to the U.S. by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses (SCCs). In March 2022, the U.S. and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU-U.S. Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for United States Signals Intelligence Activities. European court and regulatory decisions subsequent to the CJEU decision of July 2020 have taken a restrictive approach to international data transfers. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results. From January 1, 2021, companies have had to comply with the GDPR and also the United Kingdom GDPR (UK GDPR), which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR (i.e., fines up to the greater of €20 million (£17.5 million) or 4% of global turnover). As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure, or perceived failure, by us to comply with or make effective modifications to our policies, or to comply with any federal, state or international privacy, data-retention or data-protection-related laws, regulations, orders or industry self-regulatory principles could result in proceedings or actions against us by governmental entities or others, a loss of customer confidence, damage to our brand and reputation and a loss of customers, any of which could have an adverse effect on our business. In addition, various federal, state and foreign legislative or regulatory bodies may enact new or additional laws and regulations concerning privacy, data-retention and data-protection issues, including laws or regulations mandating disclosure to domestic or international law enforcement bodies, which could adversely impact our business or our reputation with customers. For example, some countries have adopted laws mandating that some personal information regarding customers in their country be maintained solely in their country. Having to maintain local data centers and redesign product, service and business operations to limit personal information processing to within individual countries could increase our operating costs significantly.

Our employees and independent contractors, including principal investigators, consultants, commercial collaborators, service providers and other vendors, may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our results of operations.

We are exposed to the risk that our employees and independent contractors, including principal investigators, consultants, any future commercial collaborators, service providers and other vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or other unauthorized activities that violate the laws and regulations of the FDA and other similar regulatory bodies, including those laws that require the reporting of true, complete and accurate information to such regulatory bodies; manufacturing standards; U.S. federal and state healthcare fraud and abuse, data privacy laws and other similar non-U.S. laws; or laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, 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 governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. 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 and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Our business involves the use of hazardous materials, and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product and product candidates and other hazardous compounds. We and any third-party manufacturers and suppliers we engage 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 and radioactive materials. Our operations also produce hazardous waste. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our third-party manufacturers' facilities pending their use and disposal. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products.

Although we believe that the safety procedures utilized by us and our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. 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. In such an event, we may be held liable for any resulting damages; such liability could exceed our resources, and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development and manufacturing 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 that 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 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, results of operations and financial condition.

Our business may be materially adversely affected by a public health crisis such as the ongoing COVID-19 pandemic, including a resurgence of the COVID-19 pandemic or localized outbreaks in certain parts of the world.

While the COVID-19 pandemic did not materially adversely affect our business operations during the year ended December 31, 2022, economic and health conditions in the United States and across most of the globe have changed considerably since the pandemic began. In particular, supply chain disruptions have become a concern for many businesses, particularly if critical supplies are sourced from China or other regions where extended lock-downs remain a real possibility. The COVID-19 pandemic also caused significant volatility in the U.S. and international markets and was a contributing factor to high inflation and extended economic downturn. We are subject to inflationary pressures on employee wages, salaries, and the cost of various goods and services that can negatively impact our financial results. We have experienced minor delays in delivery of various products related to our manufacturing processes and in some cases have had to identify new suppliers, which at times resulted in increased costs. While none of the disruptions of our supply chain to date have been material, we cannot exclude the possibility that further supply chain disruptions due to a resurgence of the COVID-19 pandemic, even if limited to localized outbreaks in certain parts of the world, could have a material adverse effect on our business, and the extent to which these issues will impact our results remains uncertain. Moreover, the emergence of any new pandemic or similar public health crisis would subject our business to risks similar to those of the COVID-19 pandemic.

In addition to the risk of such supply chain disruptions, as a result of the COVID-19 pandemic, including a resurgence or localized outbreaks in certain parts of the world, we may also experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- We are conducting a number of clinical trials for product candidates in geographies that have been heavily affected by the COVID-19 pandemic. While the availability of first-generation vaccines in the United States (and other countries) have greatly improved the outlook for the pandemic, we believe that the emergence of variants of concern and/or the potential waning of the immune protection offered by existing vaccines has the potential to lead to prolonging the effects of the

pandemic, which could in turn have an impact on various aspects of our clinical trials. For example, with respect to clinical trials for our tumor-specific immunotherapy product candidates, investigators may not want to screen or treat cancer patients with our experimental vaccine and potentially expose them to the novel coronavirus during additional clinic visits. Other potential impacts of the COVID-19 pandemic on our various clinical trials include delays or difficulties in any planned clinical site initiation, including difficulties in obtaining IRB or ethics committee approvals, recruiting clinical site investigators and clinical site staff, delays or difficulties in enrolling patients, interruption of planned key clinical trial activities, such as clinical trial site data monitoring due to diversion of resources at clinical sites or limitation on travel imposed by federal or state governments. This may impact the integrity of subject data.

- While chimpanzee-based adenoviral (ChAd) vaccines have not yet been approved in the US, there is a risk that patient candidates to our GRANITE or SLATE vaccine candidates may become ineligible due to pre-existing neutralizing antibodies to ChAd vaccines, for example following participation in SARS-CoV-2 clinical trials using such vaccines. This in turn could slow down recruitment to our clinical trials, especially if we were to consider expanding our trials in the EU, and, ultimately, if these ChAd vaccines against SARS-CoV-2 are proven effective and become widely available in the general population, may render our vaccination approach unsuitable for many cancer patients. Similarly, patients who have been previously vaccinated with a mRNA-based vaccine may be reluctant to receive our samRNA vaccines or may have contraindications, such as allergic reaction to their SARS-CoV-2, mRNA-based vaccines.

- Our increased reliance on personnel working from home, a shift that began with the COVID-19 pandemic but has become the established norm, may negatively impact productivity or disrupt, delay or otherwise adversely impact our business. In addition, this could increase our cyber-security risk, create data accessibility concerns and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites, research or clinical trial sites and important agencies and contractors.

- The FDA and comparable foreign regulatory agencies may experience operational interruptions or delays, which may impact timelines for regulatory submission, trial initiation and regulatory approval.

The COVID-19 outbreak has become less of a direct threat to public health in countries that have achieved relatively high vaccination rates, such as the United States; but, it remains unclear when the pandemic will cease to pose a threat to the global economy, particularly if full global vaccination is not achieved or existing vaccines prove less effective against new variants of the virus. The extent to which the outbreak may impact our business, manufacturing, preclinical development activities, preclinical studies and planned clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the potential for localized outbreaks of COVID-19 in countries or regions with relatively low vaccination rates, travel restrictions, lock-downs and other actions to contain the outbreak or treat its impact, business closures or business disruptions, and the effectiveness of actions taken to contain and treat the disease.

Risks Related to Intellectual Property

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates, proprietary technologies and their uses that are important to our business. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our product candidates and proprietary technologies and erode or negate any competitive advantage we may have, which could have a material adverse effect on our financial condition and results of operations.

We have applied, and we intend to continue applying, for patents covering aspects of our product candidates, proprietary technologies and their uses that we deem appropriate. However, we may not be able to apply for patents on certain aspects of our current or future product candidates, proprietary technologies and their uses in a timely fashion, at a reasonable cost, in all jurisdictions, or at

all, and any potential patent coverage we obtain may not be sufficient to prevent substantial competition. As of December 31, 2022, our solely owned patent portfolio includes pending patent applications and issued patents. We cannot be certain that the claims in any of our patent applications will be considered patentable by the United States Patent and Trademark Office (USPTO) courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued patents will not be found invalid or unenforceable if challenged. The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our actual or potential future collaborators will be successful in protecting our product candidates, proprietary technologies and their uses by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;

- patent applications may not result in any patents being issued;

- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;

- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential product candidates;

- other parties may have designed around our claims or developed technologies that may be related or competitive to our platform, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications, either by claiming the same methods or devices or by claiming subject matter that could dominate our patent position;

- any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary for the practice of our technologies or the successful commercialization of any products or product candidates that we may develop;

- because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates, proprietary technologies and their uses;

- an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications for any application with an effective filing date before March 16, 2013;

- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and

- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

The patent position of biotechnology companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. Moreover, the patent prosecution process is also expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents, if issued, or the patent rights that we license from others, may be challenged in the courts or patent offices in the United States and abroad. Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time

third parties can raise objections against such initial grant. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical products, or limit the duration of the patent protection of our products and product candidates. 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.

Our ability to enforce our patent rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or service. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents covering our products are invalidated or found unenforceable, or if a court found that valid, enforceable patents held by third parties covered one or more of our products, our competitive position could be harmed, or we could be required to incur significant expenses to enforce or defend our rights. If we initiate lawsuits to protect or enforce our patents, or litigate against third-party claims, such proceedings would be expensive and would divert the attention of our management and technical personnel.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our products;
- any of our pending patent applications or those of our licensors may issue as patents;
- others will not or may not be able to make, use, offer to sell, or sell products that are the same as or similar to our own but that are not covered by the claims of the patents that we own or license;
- we will be able to successfully commercialize our products, if approved, on a substantial scale before the relevant patents that we own or license expire;
- we were the first to make the inventions covered by each of the patents and pending patent applications that we own or license;
- we or our licensors were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe the patents we own or license;
- any of the patents we own or license will be found to ultimately be valid and enforceable;
- any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable products or will provide us with any competitive advantages;
- a third party may not challenge the patents we own or license and, if challenged, a court would hold that such patents are valid, enforceable and infringed;
- we may develop or in-license additional proprietary technologies that are patentable;
- the patents of others will not have an adverse effect on our business;
- our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we will develop additional proprietary technologies or products that are separately patentable; or

- our commercial activities or products will not infringe upon the patents of others.

Where we obtain licenses from or collaborate with third parties, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties, or such activities, if controlled by us, may require the input of such third parties. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Moreover, if we do obtain necessary licenses, we will likely have obligations under those licenses, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license, or expiration of licensed patents or patent applications, could have a material adverse impact on our business.

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

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its first effective non-provisional filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates, proprietary technologies and their uses are obtained, once the patent life has expired, we may be open to competition. In addition, although upon issuance in the United States a patent's life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. 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. If we do not have sufficient patent life to protect our product candidates, proprietary technologies and their uses, our business and results of operations will be adversely affected.

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

We rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information. We have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and technological security measures. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and 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. In addition, such security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant, customer or third party with authorized access. Our security measures may not prevent an employee, consultant or customer from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time-consuming, and the outcome is unpredictable. Even though we use commonly accepted security measures, the criteria for protection of trade secrets can vary among different jurisdictions.

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, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. Though our agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third-party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such a competitor from using that technology or information to compete with us, which could harm our competitive position. Because from time to time we expect to rely on third parties in the development, manufacture, and distribution of our products and provision of our services, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs, or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced, and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by other companies. The patent protection, prosecution and enforcement for some of our product candidates may be dependent on third parties.

We currently are reliant upon licenses of certain patent rights and proprietary technology from third parties that is important or necessary to the development of our technology and products, including technology related to our product candidates. For example, we rely on our license agreements with Arbutus and Genevant for certain lipid nanoparticle-based delivery technologies. These and other licenses we may enter into in the future may not provide adequate rights to use such intellectual property and technology in all relevant fields of use or in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to develop and commercialize our technology and products in fields of use and territories for which we are not granted rights pursuant to such licenses.

Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition.

In some circumstances, we may not have the right to control the preparation, filing, prosecution and enforcement of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, some of our agreements with our licensors require us to obtain consent from the licensor before we can enforce patent rights, and our licensor may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that our licensors or collaborators will prosecute, maintain, enforce and defend such intellectual property rights in a manner consistent with the best interests of our business, including by taking reasonable measures to protect the confidentiality of know-how and trade secrets, or by paying all applicable prosecution and maintenance fees related to intellectual property registrations for any of our product candidates. We also cannot be certain that our licensors have drafted or prosecuted the patents and patent applications licensed to us in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. If they fail to do so, this could cause us to lose rights in any applicable intellectual property that we in-license, and as a result our ability to develop and commercialize products or product candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing products.

Our licensed European patents and patent applications could be challenged in the recently created Unified Patent Court (UPC) for the European Union, that is expected to be fully ratified in 2023. Under our current license agreements, we may not have the final or sole decision on whether we are able to opt out certain of our in-licensed European patents and patent applications from the recently created Unified Patent Court (UPC) for the European Union, that is expected to be fully ratified in 2023. Our licensors may decide to not opt out of the UPC, which would subject our in-licensed European patents and patent applications to the jurisdiction of the UPC. Furthermore, even if our licensors decide to opt out of the UPC, we cannot guarantee that our licensors will comply with the legal formalities and requirements for properly opting out of the UPC. Thus, we cannot be certain that our in-licensed European patents and patent applications will not fall under the jurisdiction of the UPC. Under the UPC, a single European patent would be valid and enforceable in numerous European countries. A challenge to the validity of a European patent under the UPC, if successful, could result in a loss of patent protection in numerous European countries which could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

Our current licenses impose, and our future licenses likely will impose, various royalty payments, milestones, and other obligations on us. If we fail to comply with any of these obligations, we may be required to pay damages and the licensor may have the right to terminate the license. Termination by the licensor would cause us to lose valuable rights and could prevent us from developing and commercializing our product candidates and proprietary technologies. Our business would suffer if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Furthermore, if any current or future licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical to ours. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

Litigation or other proceedings or third-party claims of intellectual property infringement could require us to spend significant time and money and could prevent us from selling our products.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts. We cannot assure you that our operations do not, or will not in the future, infringe existing or future patents.

Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and future approved products or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, reexaminations, inter partes review proceedings and post-grant review proceedings before the USPTO and/or corresponding foreign patent offices. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. For example, we are aware of and have timely opposed EP Patent 2569633, expiring in May 2031 (absent any patent term adjustments or extensions), directed to certain methods of identifying and using neoantigens. EP Patent 2569633 is currently validated in Great Britain, France, Germany, Netherlands, Italy, Ireland, Spain and Switzerland. Our opposition was filed in our name on November 7, 2016 by Vossius & Partner. Four other parties also filed oppositions to the patent within the required timeframe. The Opposition Division of the European Patent Office (EPO), held opposition hearings on October 15 and 16, 2018, and determined that EP Patent 2569633 does not meet the requirements of the European Patent Convention (EPC) and consequently, revoked the patent. We received notice in April 2019 that EP Patent 2569633 patentees and licensors filed their appeal to the Opposition Division's decision, and we, along with other opposers, filed responses in August 2019. Opponent Christian Müller withdrew his opposition in May 2020, but the appeal proceedings were to be continued between the remaining parties. The EPO scheduled the oral proceedings for the appeal for September 27 and 28, 2022. However, on August 22, 2022, Appellant filed for withdrawal of their appeal and the oral proceedings were subsequently cancelled. The Opposition Division's decision revoking EP Patent 2569633 is thus final.

Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history and can involve other factors such as expert opinion. Our interpretation of the relevance or the scope of claims in a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. Further, we may incorrectly determine that our technologies, products, or product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our products or product candidates.

As the biotechnology industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates. We do not always conduct independent reviews of pending patent applications of, and patents issued to, third parties.

Patent applications in the United States and elsewhere are typically published approximately eighteen (18) months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Certain U.S. applications that will not be filed outside the United States can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates. As such, there may be applications of others now pending or recently revived patents of which we are unaware. These applications may later result in issued patents, or the revival of previously abandoned patents, that will prevent, limit or otherwise interfere with our ability to make, use or sell our products. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published, we may be unaware of third-party patents that may be infringed by commercialization of our product candidates, and we cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty

in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing our product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- require us to pay damages to the party whose intellectual property rights we may be found to be infringing, which may include treble damages if we are found to have been willfully infringing such intellectual property;
- require us to pay the attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be infringing; and/or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all.

Although no third party has asserted a claim of patent infringement against us as of the date of this report, others may hold proprietary rights that could prevent any of our immunotherapy candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidates or processes could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market the affected immunotherapy candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Even if such licenses are available, we could incur substantial costs related to royalty payments for licenses obtained from third parties, which could negatively affect our gross margins, and the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. In addition, we cannot be certain that we could redesign our product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our immunotherapy candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology.

If we collaborate with third parties in the development of technology in the future, our collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. Also, we may be obligated under our agreements with our collaborators, licensors, suppliers and others to indemnify and hold them harmless for damages arising from intellectual property infringement by us.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

Competitors may infringe our intellectual property rights or those of our licensors. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in a patent infringement proceeding, a court may decide that a patent we own or in-license is not valid, is unenforceable and/or is not infringed. If we or any of our potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar

claims before the USPTO, even outside the context of litigation. For example, third parties may petition the USPTO for post-grant review within nine (9) months of our patent's issuance date. Further, after the USPTO period for filing post-grant review has expired, third parties may file a petition for inter partes review on certain grounds. Similar mechanisms for challenging the validity and enforceability of a patent exist in ex-U.S. patent offices and may result in the revocation, cancellation, or amendment of any ex-U.S. patents we hold in the future. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses and could distract 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, 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

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. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will depend in part on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a 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. These established companies may have a competitive advantage over us due to their size, cash 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.

We have collaborated with U.S. academic institutions and may in the future collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. These institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

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 that program and our business and financial condition could suffer.

We may fail to comply with any of our obligations under existing or future agreements pursuant to which we license or have otherwise acquired intellectual property rights or technology, which could result in the loss of rights or technology that are material to our business.

We are party to various agreements that we depend on to operate our business, including intellectual property rights relating to GRANITE, SLATE and CORAL, in particular, our agreements with Arbutus and Genevant. Our rights to use currently licensed intellectual property or intellectual property to be licensed in the future are subject to the continuation of and our compliance with the terms of these agreements. Disputes may arise regarding our rights to intellectual property licensed to us from a third party, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the creation or use of intellectual property by us, alone or with our licensors and collaborators;
- the scope and duration of our payment obligations;
- our rights upon termination of such agreement; and
- the scope and duration of exclusivity obligations of each party to the agreement.

If disputes over intellectual property and other rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current license agreements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. If we fail to comply with our obligations under current or future license agreements, these agreements may be terminated or the scope of our rights under them may be reduced and we might be unable to develop, manufacture or market any product that is licensed under these agreements.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the biotechnology and biopharmaceutical industries, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or biopharmaceutical companies including our competitors or potential competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team.

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

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. In addition, we may face claims by third parties that our agreements with employees, contractors or consultants obligating them to assign intellectual property to us are ineffective or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and interfere with our ability to capture the commercial value of such intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even

if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees.

If we do not obtain patent term extension for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of GRANITE, SLATE, CORAL or any future immunotherapy candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

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 or customers in our markets of interest. At times, competitors 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 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. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and trade names by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, 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 financial condition or results of operations.

Changes in patent law in the U.S. or in other countries could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

Our patent rights may be affected by developments or uncertainty in U.S. or ex-U.S. patent statutes, patent case laws in USPTO rules and regulations or in the rules and regulations of ex-U.S. patent offices. There are a number of changes to the U.S. patent laws that may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, on September 16, 2011, the Leahy-Smith America Invents Act (Leahy-Smith Act) was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a “first to file” system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post-grant proceedings including opposition, derivation, reexamination, inter partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. This could have a negative impact on some of our intellectual property and could increase uncertainties surrounding obtaining and enforcement or defense of our issued patents. In addition, Congress may pass patent reform legislation that is unfavorable to us. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening 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 value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

Similarly, statutory or judicial changes to the patent laws of other countries may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Our European patents and patent applications could be challenged in the recently created Unified Patent Court (UPC) for the European Union, that is expected to be fully ratified in 2023. We may decide to opt out our European patents and patent applications from the UPC. However, if certain formalities and requirements are not met, our European patents and patent applications could be challenged for non-compliance and brought under the jurisdiction of the UPC. We cannot be certain that our European patents and patent applications will avoid falling under the jurisdiction of the UPC, if we decide to opt out of the UPC. Under the UPC, a granted European patent would be valid and enforceable in numerous European countries. Although such patent rights would apply to numerous European countries, a successful challenge to a European patent under the UPC could result in loss of patent protection in numerous European countries. Accordingly, a single proceeding under the UPC addressing the validity and infringement of the European patent could result in loss of patent protection in numerous European countries rather than in each validated country separately as such patents always have been adjudicated. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates

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

Filing, prosecuting and defending all current and future patents 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 some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but 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.

The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights. For example, some foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, some countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Proceedings to enforce our patent 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. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We employ reputable professionals and rely on such third parties to help us comply with these requirements and effect payment of these fees with respect to the patents and patent applications that we own, and if we license intellectual property we may have to rely upon our licensors to comply with these requirements and effect payment of these fees with respect to any patents and patent applications that we license. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

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

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:

- others may be able to make next generation cancer and infectious disease immunotherapies that are similar to ours but that are not covered by the claims of the patents that we own or have exclusively licensed;

- we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- 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 may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

Risks Related to Government Regulation

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.

If one or more of our product candidates is approved, each will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP or similar regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP or similar regulations and adherence to commitments made in any approved marketing application. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs and biologics are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label and truthful and non-misleading. As such, we may not promote our products "off-label" for indications or uses for which they do not have approval. The holder of an approved application must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical studies to verify the safety and efficacy of our products in general or in specific patient subsets. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval.

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

- issue warning letters;
- impose civil or criminal penalties;

- suspend, vary or revoke regulatory approval;
- suspend any of our clinical studies;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products, or require or request a product recall.

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

Moreover, the policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, the CARES Act made a number of changes to the Federal Food, Drug and Cosmetic Act aimed at preventing drug shortages. Similarly, the FDA has issued a number of guidance documents describing the agency's expectations for how drug manufacturers should comply with various FDA requirements during the pandemic, including with respect to conducting clinical trials, distributing drug samples, and reporting post-marketing adverse events. Moreover, as a result of the COVID-19 pandemic, there has been increasing political and regulatory scrutiny of foreign-sourced drugs and foreign drug supply chains, resulting in proposed and enacted legislative and executive actions, including Executive Orders, to incentivize or compel drug manufacturing operations to relocate to the United States. It is not clear how these changes and proposals could impact our business. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability.

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

We may pursue orphan drug designation for certain of our future product candidates. Under the Orphan Drug Act, the FDA may designate a drug or biologic product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the European Commission, on the basis of a scientific opinion by the EMA's Committee for Orphan Medicinal Products (COMP), grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product. In any event, orphan designation is granted only if there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition. It is no longer necessary to obtain orphan designation in Great Britain before an application for marketing authorization is made, and the criteria will be assessed by the MHRA, at the time of assessment of the application for marketing authorization. The criteria in Great Britain are similar to those in the EU but have been tailored for the Great Britain market.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax credits for certain clinical trial costs, and application fee waivers. In addition, if an orphan-designated product receives the first FDA approval for the indication for which it has orphan designation (meaning that FDA has not previously approved a drug considered the same drug for same orphan condition), the product is entitled to orphan drug exclusivity. If there is a previously approved same drug for the same orphan condition, to obtain orphan exclusivity, the sponsor of the subsequent drug must demonstrate clinical superiority over the previously approved same drug. If granted, orphan exclusivity means the FDA may not approve any other application to market the same drug for the same disease or condition for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity to meet the needs of the orphan patient population. In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval, subject to the positive outcome of the reassessment of the continued compliance with the orphan designation criteria at the time of approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met at the

end of the fifth year since grant of the approval, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Moreover, upcoming legislative reforms in the European Union may result in a reduction of market exclusivity periods for orphan medicinal products and/or imposition of additional requirements for grant of such exclusivity. In Great Britain, if the criteria for orphan designation are met at the time of assessment of the marketing authorization, the applicant is entitled to a fee reduction and ten years of market exclusivity. The terms of market exclusivity, and possibility for the period to be reduced, are similar to those in the EU. The European Commission is expected to publish new proposed legislation in March 2023 which, if adopted by the European Parliament and the Council of Ministers, will introduce significant number of changes to the market exclusivities granted to orphan medicinal products and the related procedures and requirements in the EU.

Even if we obtain orphan drug designation for a product candidate, we may not be the first to obtain marketing approval for the product candidate for any particular orphan indication due to the uncertainties associated with developing novel biologic products. Further, even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA or foreign regulatory authorities can subsequently approve the same drug with the same active moiety for the same condition if the FDA or foreign regulatory authorities concludes that the later drug is clinically superior in that it is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug or biologic nor gives the drug or biologic any advantage in the regulatory review or approval process.

Moreover, a September 2021 Eleventh Circuit decision in *Catalyst Pharmaceuticals, Inc. vs. Becerra* regarding interpretation of the Orphan Drug Act exclusivity provisions as applied to drugs approved for orphan indications narrower than the drug's orphan designation could significantly broaden the scope of orphan drug exclusivity for such products. In January 2023, FDA, however, issued a Federal Register notice clarifying its approach to orphan drug exclusivity following the *Catalyst* decision that suggests this may not be the agency's intended direction going forward. Consistent with the court's decision, FDA set aside its approval of the drug at issue in the case. But otherwise, the notification announced that at this time, while complying with the court's order in *Catalyst*, FDA intends to continue to apply its regulations tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved to matters beyond the scope of that order. Specifically, FDA intends to continue to apply its longstanding regulations tying the scope of orphan drug exclusivity to the uses or indications for which the orphan drug was approved. Legislation also has been introduced that may reverse the Catalyst decision.

A fast track designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

We have received fast track designation for GRANITE for the treatment of colorectal cancer, and we may seek such designation for some or all of our other product candidates. If a drug or biologic, in our case, is intended for the treatment of a serious or life-threatening disease or condition and the biologic demonstrates the potential to address unmet medical needs for this disease or condition, the biologic sponsor may apply for FDA fast track designation. The sponsor of a fast-track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development; and, once a BLA is submitted, the product candidate may be eligible for priority review. A fast track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA. The FDA has broad discretion whether or not to grant this designation. Even if we believe a particular product candidate is eligible for this designation, we cannot guarantee that the FDA would grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

Some of our product candidates may require pediatric development, which may delay our regulatory approvals and ultimately our commercial licensure.

The RACE for Children Act enacted in the U.S. in August 2017 and the European Pediatric Regulation implemented in 2007 as well as similar legislation in the UK may require us to develop our products in pediatric cancer patients. Pediatric cancers are rare, mutational burden is usually low in pediatric tumors and our approach may not be suited for children with cancer, or it may be difficult and slow to accrue children with cancers in our clinical trials. We may incur delays in meeting potential regulatory obligations or require additional investments to fulfill our regulatory commitments, and ultimately may be found incompliant if we cannot deliver pediatric data within the agreed timelines. This could lead to delays in regulatory approval and ultimately commercial licensure of our GRANITE or SLATE products.

Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

In the United States, the European Union and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the ACA was enacted, which substantially changed the way healthcare is financed by both governmental and private payors. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a licensure framework for follow on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Furthermore, the expansion of the 340B Drug Discount Program through the ACA has increased the number of purchasers who are eligible for significant discounts on branded drugs. Several drug manufacturers have commenced litigation, which remains ongoing, challenging the legality of contract pharmacy arrangements under the 340B Drug Discount Program, which may affect the way in which manufacturers are required to extend the 340B Drug Discount Program prices to covered entities, including through contract pharmacies. There are also ongoing challenges regarding the implementation of the 340B Drug Discount Program Administrative Dispute Resolution Process, which is in part intended to resolve claims by covered entities that they have been overcharged for covered outpatient drugs by manufacturers. In November 2022, the Health Resources and Services Administration issued a proposed rule to establish and implement an administrative dispute resolution process for certain disputes arising hunder the 340B drug pricing program. The public comment period closed on January 30, 2023. The nature of the Administrative Dispute Resolution Process, once finalized, may have a material adverse impact on our revenue should we participate in the 340B Drug Discount Program after receiving approval for our product candidates.

Since its enactment, there have been judicial, Congressional, and executive branch challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed a recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace during the COVID-19 pandemic. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted, including aggregate reductions of Medicare payments to providers, which went into effect April 1, 2013 and due to subsequent legislative amendments, will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, absent further congressional action. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers and accordingly, our financial operations. Additionally, Congress has considered a number of bills relating to drug pricing and recently enacted the Inflation Reduction Act of 2022 (IRA), which was signed into law by President Biden and contains a number of provisions regarding drug pricing. The IRA adopted drug pricing reforms that

will allow the federal government to negotiate prices for some high-cost drugs covered under Medicare Parts B and D, introduce inflationary rebates on certain Medicare Part B and Medicare Part D drugs and redesign the structure of the Part D benefit. It remains unclear how numerous aspects of this law will be implemented and how it will affect our business, and it is possible that Congress will consider other legislation that would affect drug pricing issues going forward. Although the Build Back Better Act stalled in Congress, there are other drug pricing reforms still under consideration in Congress, including elements of the Build Back Better Act aimed at allowing Medicare to negotiate the price of prescription drugs in the United States.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries, hearings and proposed and enacted federal legislation and rules, as well as Executive Orders, designed to, among other things, reduce or limit the prices of drugs and make them more affordable for patients, such as by tying the prices that Medicare reimburses for physician-administered drugs to the prices of drugs in other countries, bring more transparency to drug pricing rationale and methodologies (including, for example, by requiring drug manufacturers to disclose planned drug price increases and the rationales for such increases), implement data collection and reporting under Section 204 of Title II of Division BB of the Consolidated Appropriations Act, 2021, which requires, among other things, health plans and issuers to disclose rebates, fees, and other remuneration provided by drug manufacturers related to certain pharmaceutical products, revise rules associated with the calculation of Medicaid Average Manufacturer Price and Best Price, including the removal of the current statutory 100% of Average Manufacturer Price per-unit cap on Medicaid rebate liability for single source and innovator multiple source drugs effective as of January 1, 2024 under the American Rescue Plan Act of 2021, which may significantly affect the amount of rebates paid on prescription drugs under Medicaid and the prices that are required to be charged to covered entities under the 340B Drug Discount Program, and facilitate the importation of certain lower-cost drugs from other countries. In July 2021, President Biden issued an Executive Order directing various executive branch agencies to take actions to lower drug prices and promote generic competition, including directing FDA to support and work with states and Indian Tribes to develop importation plans to import prescription drugs from Canada. The Executive Order required the Secretary of Health and Human Services to develop a comprehensive plan for addressing drug prices. The plan was released on September 9, 2021, and it includes support for legislative and administrative actions that would improve affordability, access and competition, and foster scientific innovation. Following passage of the IRA, in October 2022, President Biden issued an Executive Order directing the Center for Medicare and Medicaid Innovation to consider new models to lower drug costs and promote access to Medicare and Medicaid beneficiaries. The Executive Order directs HHS to issue a report on potential models to the White House within 90 days, and HHS delivered a report to President Biden on February 14, 2023 that outlines three models, including one that would develop payment methods for drugs approved under accelerated approval, in consultation with the Food and Drug Administration, to encourage timely confirmatory trial completion and improve access to post market safety and efficacy data. It is possible that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the European Union and UK, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. Moreover, upcoming legislative and policy changes in the European Union may further impact the price and reimbursement status of our products in the future.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under any U.S. federal healthcare program, such as Medicare and Medicaid. 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 U.S. federal civil and criminal false claims and civil monetary penalties laws, including the civil False Claims Act, which prohibit, among other things, including through civil whistleblower or qui tam actions, individuals or entities from knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;

- HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation;

- the Food, Drug and Cosmetic Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;

- the U.S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product;

- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the government information related to certain payments and other transfers of value to physicians (as defined by statute), certain non-physician practitioners such as physician assistants and nurse practitioners, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws requiring the registration of pharmaceutical sales representatives;

- the U.S. Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, U.S. companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office, and foreign political parties or officials thereof; and

- similar healthcare laws and regulations in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Risks Related to Our Common Stock

Our stock price is volatile, and you may not be able to resell shares of our common stock at or above the price you paid.

The trading price of our common stock is highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include those discussed in this “Risk Factors” section of this report and others such as:

- results from, and any delays in, our clinical trials, in particular for GRANITE and SLATE or any other current or future clinical development programs, including public misperception of the results of our trials;

- announcements by academic or other third parties challenging the fundamental premises underlying our approach to treating cancer and infectious disease and/or biopharmaceutical product development;

- announcements of regulatory approval or disapproval of our current or any future product candidates;

- failure or discontinuation of any of our research and development programs;

- manufacturing setbacks or delays of or issues with the supply of the materials for our personalized immunotherapy candidate;

- announcements relating to future licensing, collaboration or development agreements, including the early termination or failure of an existing strategic collaboration;

- delays in the commercialization of our current or any future product candidates;

- public misperception regarding the use of our therapies;

- acquisitions and sales of new products, technologies or businesses;

- quarterly variations in our results of operations or those of our current or future competitors;

- changes in earnings estimates or recommendations by securities analysts;

- announcements by us or our competitors of new products, significant contracts, commercial relationships, acquisitions or capital commitments;
- developments with respect to intellectual property rights;
- our commencement of, or involvement in, litigation;
- changes in financial estimates or guidance, including our ability to meet our future revenue and operating profit or loss estimates or guidance;
- any major changes in our board of directors or management;
- new legislation, particularly in the United States, relating to the sale or pricing of pharmaceuticals;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry;
- product liability claims or other litigation or public concern about the safety of our product candidates;
- market conditions in the biopharmaceutical and biotechnology sectors, particularly as a result of the volatility in the market caused by the COVID-19 pandemic; and
- general economic conditions in the United States and abroad.

In addition, the stock markets in general, and the markets for biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of any particular issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit, and the attention of our management would be diverted from the operation of our business.

The future issuance of equity or of debt securities that are convertible into equity will dilute our share capital.

We may choose to raise additional capital in the future, depending on market conditions, strategic considerations and operational requirements. For example, we have issued and may continue to issue shares in our “at the market offering” program or other registered offerings under our 2022 Shelf Registration Statement, and we have issued shares in three private placement of public issuer’s equity transactions. To the extent that additional capital is raised through the issuance of shares of common stock or other securities convertible into shares of common stock, our stockholders will be diluted. In addition, future issuances of our common stock or other equity securities (or securities convertible into our common stock or other equity securities), or the perception that such sales may occur, could adversely affect the trading price of our common stock and impair our ability to raise capital through future offerings of shares or other securities.

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

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of December 31, 2022, we have a total of 86,894,901 shares of common stock outstanding, as well as approximately 26.8 million shares underlying pre-funded warrants and approximately 7.7 million shares of common stock that are subject to outstanding options, restricted stock units or other equity awards. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future, 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, until such unused losses expire, if ever. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (IRC), if a corporation undergoes an “ownership change,” generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. Any equity financing transactions, private placements and other transactions that occur within

a three-year testing period may trigger additional ownership changes, which could further limit our use of such tax attributes. Any such limitations, whether as a result of prior or future offerings of our common stock or sales of common stock by existing stockholders, could have an adverse effect on our results of operations in our future years.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent changes in control or changes in our management without the consent of our board of directors. These provisions include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to alter our amended and restated bylaws without obtaining stockholder approval;
- the required approval of at least 66 2/3% of the shares entitled to vote at an election of directors to adopt, amend or repeal our amended and restated bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which force stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by our chief executive officer or president or by the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Our amended and restated certificate of incorporation and our amended and restated bylaws provide for an exclusive forum in the Court of Chancery of the State of Delaware and in the U.S. federal district courts for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation and our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. The exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts

have exclusive jurisdiction. In addition, our amended and restated certificate of incorporation provides that the U.S. federal district courts are the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Our exclusive forum provision will not relieve us of our duties to comply with the federal securities laws and the rules and regulations thereunder, and our stockholders will not be deemed to have waived our compliance with these laws, rules and regulations.

The 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 other employees and result in increased costs for investors to bring a claim.

Risks related to our Loan Agreement

Our failure to comply with the covenants or payment obligations under our existing term loan facility could result in an event of default, which may result in increased interest charges, acceleration of our repayment obligations or other actions by the lenders, any of which could negatively impact our business, financial condition and results of operations.

On July 19, 2022, we entered into a Loan and Security Agreement (the "Loan Agreement") with Hercules Capital, Inc., Silicon Valley Bank, and certain financial institutions or other entities from time-to-time party thereto (the "Lenders") pursuant to which the Lenders made available to us a secured term loan facility in an aggregate principal amount of up to $80 million (the "Term Loan"). We immediately drew $20.0 million under this facility upon entry into the Loan Agreement. In connection with the Loan Agreement, we granted the Lenders a security interest in substantially all of our personal property and other assets, other than our intellectual property. The Loan Agreement contains customary affirmative and restrictive covenants and representations and warranties, including a covenant against the occurrence of a change in control (as defined by the Loan Agreement), financial reporting obligations, and certain limitations on indebtedness, liens (including a negative pledge on intellectual property and other assets), investments, distributions (including dividends), collateral, investments, transfers, mergers or acquisitions, taxes, corporate changes, and deposit accounts. The Loan Agreement also includes customary events of default, including payment defaults, breaches of covenants following any applicable cure period, the occurrence of certain events that could reasonably be expected to have a material adverse effect (as set forth in the Loan Agreement), cross default to certain third-party indebtedness and certain events relating to bankruptcy or insolvency. Upon the occurrence of an event of default, a default interest rate of an additional 4.0% may be applied to the outstanding principal and interest payments due, and the Lenders may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Loan Agreement, including proceeding against the collateral securing such indebtedness. Such increased interest charges, accelerated repayment, proceedings against the collateral or other actions may have a negative impact on our business, financial condition and results of operations.

Our existing and any future indebtedness may limit our cash flow available to invest in the ongoing needs of our business.

Our outstanding debt combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- requiring us to dedicate cash flow from operations or cash on hand to the payment of interest on, and principal of, our debt, which will reduce the amounts available to fund working capital, capital expenditures, product development efforts and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and our industry; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our existing cash and funds from external sources. Nonetheless, we may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under our existing or any future debt facility. Funds from external sources may not be available on acceptable terms, if at all. In addition, a failure to comply with the covenants under the Loan Agreement or any future loan agreements we may enter into could result in an event of default and acceleration of amounts due. If an event of default occurs and the lenders accelerate the amounts due under such loan agreements, we may not be able to make accelerated payments, and such lenders could seek to enforce security interests in the collateral securing such indebtedness.

General Risk Factors

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

We incur substantial costs as a result of operating as a public company, and our management devotes substantial time to governance and compliance matters. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would harm our business.

We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Exchange Act and regulations regarding corporate governance practices. The listing requirements of the Nasdaq Global Select Market and the rules of the SEC require that we satisfy certain corporate governance requirements relating to director independence, filing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct, among other requirements. Our management and other personnel devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms or at all.

As a public company, we are subject to Section 404 of the Sarbanes-Oxley Act of 2002 (Section 404) and the related rules of the SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company as defined in the JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404. Once we are no longer an emerging growth company or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal controls over financial reporting. We will remain an emerging growth company until December 31, 2023.

In order to provide the reports required by these rules we must conduct reviews and testing of our internal controls. During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. In order to report our results of operations and financial statements on an accurate and timely basis, we will depend on third party vendors to provide timely and accurate notice of their costs to us. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Global Select Market or other adverse consequences that would materially harm our business.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities, or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.

- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.

- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.

- We will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.

- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.

- We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

We do not currently intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters are currently located at 5959 Horton Street, Emeryville, California, comprising approximately 34,600 square feet of office and laboratory space. The lease term for the 5959 Horton lease expires on November 30, 2029 and we have an option to extend the lease term for two consecutive additional terms of 5 years. We also currently lease an aggregate of 20,700 square feet of space in two Cambridge, Massachusetts facilities, including (i) the lease of approximately 13,900 square feet of office and laboratory space, the term of which expires in April 2025 and (ii) the lease of approximately 6,800 square feet of office and laboratory space, the term of which expires in June 2023.

We lease a manufacturing facility in Pleasanton, California, where we occupy approximately 42,600 square feet of space. The current term of our lease expires in November 2024, with an option to extend the term through November 2029. We also lease an additional space in Pleasanton, California, where we occupy approximately 7,100 square feet of general office space. The current term of the lease expires in November 2024.

In addition, we lease part of a newly-built facility in Boston, Massachusetts, comprising approximately 73,495 square feet of office and laboratory space. We expect to take occupancy of this facility in 2023.

For additional information on all our properties, see "Leases" in Note 6 to our consolidated financial statements.

We believe that our existing facilities are sufficient for our needs for the immediate future and that, with our new facility in Boston, our facilities will meet the anticipated needs of our business in the medium term. As we continue to grow the business, we may lease additional or alternate space, and we believe suitable additional or alternative space will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

From time to time, we may become involved in litigation or other legal proceedings. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Our common stock has been listed on the Nasdaq Global Select Market under the symbol "GRTS" since September 28, 2018. Prior to that date, there was no public trading market for our common stock.

Holders of Common Stock

As of March 7, 2023, there were 18 holders of record of our common stock. Because many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of beneficial owners of our common stock represented by these record holders.

Dividend Policy

We have never declared or paid any cash dividends on our common stock or any other securities. We anticipate that we will retain all available funds and future earnings, if any, for use in the operation of our business and do not anticipate paying cash dividends in the foreseeable future. In addition, future debt instruments may materially restrict our ability to pay dividends on our common stock. Payment of future cash dividends, if any, will be at the discretion of the board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements of current or then-existing debt instruments and other factors the board of directors deems relevant.

Performance Graph

As a "smaller reporting company" as defined by Item 10 of Regulation S-K, the Company is not required to provide this information.

Recent Sales of Unregistered Securities

Not applicable.

Use of Proceeds

Not applicable.

Issuer Purchases of Equity Securities

Not applicable.

Item 6. [Reserved]

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

You should read the following discussion and analysis of our financial condition and results of operations together with our audited financial statements and the related notes thereto included elsewhere in this Annual Report on Form 10-K. This discussion and analysis, and other parts of this report, contain forward-looking statements, including, but not limited to, statements related to the potential of our therapeutic programs. Such forward-looking statements involve substantial risks and uncertainties that could cause our research and clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements, including interim results obtained may differ from those at completion of the studies and clinical trials. Such risks and uncertainties include, among others, the uncertainties inherent in the drug development process, including our programs' early stage of development, the process of designing and conducting preclinical and clinical trials, the regulatory approval processes, the timing of regulatory filings, the challenges associated with manufacturing drug products, our ability to successfully establish, protect and defend its intellectual property and other matters that could affect the sufficiency of existing cash to fund operations. Our actual results could differ materially from those discussed in these forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to our business in general, see the section titled "Risk Factors" included elsewhere in this Annual Report on Form 10-K. These forward-looking statements speak only as of the date hereof. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason.

Overview

We are a clinical-stage biotechnology company focused on combining immunological insights with proprietary technologies and capabilities to develop next-generation vaccines. Specifically, we discover, develop, manufacture, and deliver vaccine-based immunotherapy candidates against cancer and infectious disease. Our goal is to unlock more potent and durable immunity by harnessing vaccine innovation. We aim to achieve that goal by leveraging our in-house capabilities and technologies to address the shortcomings of currently available vaccines and immunotherapies.

The immune system sits at the nexus of many diseases, and we believe that immune response modulation is core to several transformational product classes. Recent advances have pointed to T cells as being central to the success of cancer immunotherapy and critical in the elimination of virally infected cells. We believe that our scientific approach of focusing on generating antigen-specific T cells, particularly the challenging but critical cytotoxic CD8+ T cell subclass has the potential to drive transformational therapeutic and prophylactic benefits.

In oncology, we develop personalized vaccines that aim to destroy tumors through CD8+ (killer) T cell recognition of tumor cells by virtue of their surface display of neoantigens, peptides that are presented on cancer cells when certain mutations occur in tumor DNA. In infectious disease, we develop both therapeutic and prophylactic vaccines targeting both T cells and B cells. We believe we are leading the field of development and application of self-amplifying mRNA (samRNA), a rapidly-emerging platform technology. Our unique approach to immunogen design, whereby our vaccines deliver, as appropriate, whole proteins to drive neutralizing antibodies (nAbs) and/or protein fragments to drive T cell responses, has the potential to both neutralize incoming pathogens (through nAbs) and kill infected cells through CD8+ T cell recognition of foreign, pathogen-derived peptides displayed on the surface of infected cells.

Our clinical programs include GRANITE, an individualized neoantigen-based vaccine program; SLATE, an "off-the-shelf" neoantigen-based vaccine program; CORAL, a second-generation SARS-CoV-2 vaccine program; and HIV, HIV vaccine program in collaboration with Gilead Sciences, Inc.

The table below summarizes key information about our clinical-stage programs.

Program	Phase	Status	Indication(s)	Collaborator	Commercial Rights
GRANITE	2/3	Enrollment Ongoing; Treatment Ongoing	MSS-CRC* first line maintenance	—	Gritstone
GRANITE	1/2	Enrollment Complete; Treatment Ongoing	Early stage & advanced solid tumors	—	Gritstone
SLATE	2	Enrollment Ongoing; Treatment Ongoing	$KRAS^{mut}$-driven tumor types	—	Gritstone
SLATE	1/2	Complete	KRAS Advanced Solid Tumors	—	Gritstone
HIV	1	4Q2021 IND Cleared	HIV treatment/cure	Gilead Sciences	Gilead**
CORAL	1	Enrollment Complete; Treatment Ongoing	SARS-CoV-2 in South Africa	CEPI	Gritstone
CORAL	1	Enrollment Complete; Treatment Ongoing	SARS-CoV-2 booster	—	Gritstone
CORAL	1	Enrollment Complete; Treatment Ongoing	SARS-CoV-2 naïve & booster	NIAID, IDCRC	Gritstone

* MSS-CRC = microsatellite stable colorectal cancer
** Gilead is responsible for conducting a Phase 1 study

Beyond GRANITE, SLATE, CORAL and the HIV collaboration with Gilead, we continue to apply our broad set of capabilities in oncology and infectious diseases through promising preclinical work and partnerships.

COVID-19 Update

Since the COVID-19 pandemic began, providers of healthcare services have had to deal with significant strains on their operations. These strains have affected all healthcare institutions, including those where we conduct our clinical trials, with some institutions prohibiting or postponing the initiation of new clinical trials, slowing or halting enrollment in existing trials and restricting the on-site monitoring of clinical trials. Although our operations have not been materially impacted by the COVID-19 pandemic, we have experienced slowing of patient recruitment and sample collection in our ongoing clinical trials. Additionally, as a result of the COVID-19 pandemic, competition for potential patients in our trials may be further exaggerated as a result of multiple clinical site closures. To date, the COVID-19 pandemic has not materially affected our supply chain or production schedule, but further escalation of the health crisis has the potential to cause delays in our supply chain and manufacturing operations, which could materially adversely impact our business.

In response to the COVID-19 pandemic, we have implemented heightened health and safety measures designed to comply with applicable federal, state and local guidelines, and transitioned to a flexible work environment, where employees who can work from home effectively are allowed to do so. We have implemented virtual meeting and messaging technology and encourage employees to follow local health authority guidance. As the pandemic and its impacts continue to evolve, we may need to undertake additional actions that could impact our operations if required by applicable laws or regulations or if we determine such actions to be in the best interests of our employees.

Funding Sources

We have funded our operations to date primarily through sales of our convertible preferred stock, sales of our common stock in public offerings and under our “at-the-market” offering program, private placements of our common stock and pre-funded warrants, proceeds from the Loan Agreement (as defined below) and with proceeds received from our collaboration arrangements. We also have received targeted funding from charitable foundations. We do not expect to generate revenue from any product candidates that we develop until we obtain regulatory approval for one or more of such product candidates and commercialize our products or enter into additional collaboration agreements with third parties. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Our programs will require substantial additional development time and resources before we (or our collaboration partners) would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. In addition, we incur substantial costs associated with operating as a public company. We also do not yet have a sales organization or commercial infrastructure and, accordingly, we will incur significant expenses to develop a sales organization or commercial infrastructure in advance of generating any commercial product sales. As a result, we will need substantial additional capital to support our operating activities.

We currently anticipate that we will seek to fund our operations through equity or debt financings or other sources, such as additional collaboration agreements we may enter into with third parties. Adequate funding may not be available to us on acceptable terms, or at all, particularly in light of the current COVID-19 pandemic and associated economic uncertainty and potential local and/or

global economic recession. If sufficient funds on acceptable terms are not available when needed, we will be required to significantly reduce our operating expenses and delay, reduce the scope of, or eliminate one or more of our development programs. See “Liquidity and Capital Resources” below and Note 2 to the consolidated financial statements and related notes included elsewhere for additional information.

Manufacturing is a vital component of our platform approach to immunotherapy, and we have invested significantly in our manufacturing facility, which opened in November 2017. Until December 2019, we used a hybrid approach to manufacture our individualized immunotherapy, wherein certain elements of our product candidates were manufactured on an outsourced basis at qualified third-party contract manufacturing organizations (CMOs) and other elements of our product candidates were manufactured internally. Beginning in March 2020, we internalized the majority of the outsourced elements of the manufacturing process for our programs.

Since we commenced operations in August 2015, we have invested a significant portion of our efforts and financial resources in research and development activities and establishing our manufacturing facility. We have had significant operating losses since our inception, and we do not expect positive cash flows from operations in the foreseeable future (for additional information, see “Liquidity” in Note 1 to our consolidated financial statements). We do not have any products approved for sale. We expect to continue to incur net operating losses for at least the next several years as we advance our product candidates through clinical development, seek regulatory approval, prepare for and, if approved, proceed to commercialization, continue our research and development efforts and invest in our manufacturing facility.

Following our IPO, in April 2019, we completed an underwritten public offering and sold and issued an aggregate of 6,500,000 shares of common stock at a price to the public of $11.50 per share. We received aggregate net proceeds from the offering of approximately $69.7 million, after deducting underwriting discounts and commissions and offering costs.

In October 2019, we (i) filed a shelf registration statement on Form S-3 (the “2019 Shelf Registration Statement”), with the SEC covering up to $250.0 million of common stock, preferred stock, debt securities, warrants and units, and (ii) entered into a Sales Agreement with Cowen and Company, LLC (Cowen), for an “at-the market” $75.0 million in shares of our common stock (ATM Offering Program). Through December 31, 2022, we had received aggregate proceeds from our ATM Offering Program of $50.0 million, net of commissions and offering costs, pursuant to the issuance of 5,642,712 shares. During the year ended December 31, 2021, we issued and sold 3,990,869 shares of our common stock through our ATM Offering Program and received net proceeds of approximately $36.6 million. As of December 31, 2022, there are no further amounts available for issuance under the 2019 ATM Offering Program.

In December 2020, we entered into private placement transactions, pursuant to which we sold (i) an aggregate of 5,543,351 shares of common stock at a per share purchase price of $3.34, (ii) pre-funded warrants to purchase an aggregate of 27,480,719 shares of common stock, each with an exercise price of $3.34 per share of common stock (of which $3.33 per share was pre-paid by each purchaser), and (iii) an aggregate of 4,043,127 shares of common stock at a per share purchase price of $3.71. The aggregate gross cash proceeds to us for the securities sold in these private placements was $125.0 million, and related costs were $5.7 million.

On September 16, 2021, we entered into a Securities Purchase Agreement, pursuant to which we issued and sold, in an unregistered offering in reliance on an exemption from registration, an aggregate of 5,000,000 shares of common stock, par value $0.0001 per share, at a per share purchase price of $11.00 per share. We received aggregate gross proceeds of $55.0 million.

In March 2022, we filed the 2022 Shelf Registration Statement, covering the offering of up to $250.0 million of various equity and debt securities, including the sale and issuance of up to $100.0 million worth of shares of our common stock under the 2022 ATM Offering Program. As of December 31, 2022, we have received $20.1 million in gross proceeds from our 2022 ATM Offering Program and have $79.9 million available thereunder.

In July 2022, we entered into a loan and security agreement (the “Loan Agreement”) with Hercules Capital, Inc. (“Hercules”) and Silicon Valley Bank (“SVB”), which provides us with a 60-month term loan facility for the Company up to $80.0 million in borrowing capacity across five potential tranches. At the closing of the Loan Agreement, we drew $20.0 million from the first tranche, and we can draw up to an additional $10.0 million through March 2023. The remaining tranches provide up to $50.0 million borrowing capacity and become available if and when we meet certain milestones set forth in the Loan Agreement. The term loan is secured by substantially all of our assets, other than intellectual property. There are no warrants associated with the Loan Agreement. Beginning on April 1, 2023, so long as the Company’s market capitalization is equal to or less than $400.0 million, the Company is subject to a minimum liquidity requirement equal to the then outstanding balance under the Loan Agreement multiplied by 0.55 or 0.45, which multiplier depends on whether the Company achieves certain performance milestones.

In October 2022, we completed a third private placement of securities (the “Third PIPE Financing”), pursuant to which we sold an aggregate of 6,637,165 shares of common stock at a per share purchase price of $2.26 and pre-funded warrants to purchase 13,274,923

shares of common stock at a price of $2.26 per share (of which $2.2599 per share was prepaid by each purchaser). The aggregate gross cash proceeds to us for the securities sold in the Third PIPE Financing was $45.0 million, and related costs were $2.6 million.

Components of Our Operating Results

Collaboration and License and Grant Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales for the foreseeable future. For the years ended December 31, 2022, 2021, and 2020, we recognized $19.9 million, $48.2 million, $4.0 million, respectively, of revenue from the 2seventy Agreement, the Gilead Collaboration Agreement, the grant agreements with CEPI and Gates Foundation, and another small collaboration agreement. See Note 7 to our consolidated financial statements for additional information.

In the future, we expect to continue to recognize revenue from the 2seventy Agreement and the Gilead Collaboration Agreement and may generate revenue from product sales or other collaboration agreements, strategic alliances and licensing arrangements. We expect our revenue to fluctuate on a quarterly and annual basis due to the timing and amount of license fees, reimbursement of costs incurred, milestone and other payments, as well as product sales, to the extent that any are successfully commercialized. If we fail to complete the development of our product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

Operating Expenses

Research and Development Expenses

Since our inception, we have committed significant resources to our research and development activities, including conducting preclinical studies, manufacturing development efforts and related development activities for our product candidates.

Research and development activities account for a significant portion of our operating expenses. Research and development costs are expensed as incurred. These costs include:

- External research and development expenses, including:
  - expenses incurred under arrangements with third parties, including clinical research organizations, or CROs, preclinical testing organizations, CMOs, academic and non-profit institutions and consultants;
  - fees related to our license agreements;
- Internal research and development expenses, including (i) headcount-related expenses, such as salaries, payroll taxes, benefits, non-cash stock-based compensation and travel, for employees contributing to research and (ii) development activities, including the costs associated with the development of our EDGE™ platform; and
- Other expenses, which include direct and allocated expenses for laboratories, facilities and other costs.

Pursuant to our Arbutus License Agreement, Arbutus granted us a worldwide, exclusive license to certain technology of Arbutus, including Arbutus' portfolio of proprietary and clinically-validated LNP products and associated intellectual property, as well as technology transfer of Arbutus' manufacturing know-how.

Pursuant to our 2020 Genevant License Agreement, Genevant granted us exclusive license rights under certain intellectual property related to Genevant's LNP technology for a single indication, and we agreed to pay Genevant an initial payment of $2.0 million, and up to an aggregate of $71.0 million in specified development, regulatory, and commercial milestones, and low to mid-single digit royalties on net sales of licensed products. The upfront payment of $2.0 million was included in research and development expenses during 2020. In March 2022, a milestone in the amount of $1.0 million was met, which was included in research and development expense for the year ended December 31, 2022.

Pursuant to our 2021 Genevant License Agreement, we obtained a nonexclusive license to Genevant's LNP technology to develop and commercialize self-amplifying RNA, or samRNA, vaccines against SARS-CoV-2, the virus that causes COVID-19. Under the 2021 Genevant License Agreement, we made a $1.5 million upfront payment to Genevant, and Genevant is eligible to receive from us up to $141.0 million in contingent milestone payments per product, plus certain royalties on future product sales or licensing (or, in certain scenarios and subject to certain conditions, in lieu of these milestones and royalties Genevant would receive a percentage of amounts we receive from sublicenses). In March 2021, a milestone was met following the initial patient treatment in the Phase 1 clinical

trial conducted through the NIAID-supported IDCRC. Both the $1.5 million upfront and $1.0 million milestone payments were recorded as research and development expense for the year ended December 31, 2021. No research and development expense was recorded for the year ended December 31, 2022.

We expect our research and development expenses to increase substantially in the future as we continue to advance our product candidates into and through clinical studies and pursue regulatory approval. Such activities are costly and time-consuming and we expect our clinical studies to generally become larger and more costly to conduct as they advance into later stages. The successful development of our product candidates is highly uncertain. The actual probability of success for our product candidates may be affected by a variety of risks and uncertainties associated with drug development, including those described in the section entitled "*Risk Factors*" included in Part II, Section 1A and elsewhere in this report.

The following table summarizes our research and development expenses by program and category (in thousands):

	Year Ended December 31,	
	2022	2021
GRANITE program external expenses	$ 13,832	$ 11,962
SLATE program external expenses	2,691	3,706
CORAL program external expenses	12,082	4,879
Other program external research and development expenses	23,403	26,362
Personnel-related expenses [(1)]	42,030	34,138
Other unallocated research and development expenses	17,365	16,443
Total research and development expenses	$ 111,403	$ 97,490

[(1)] Personnel-related expenses include stock-based compensation expense of $6.7 million and $6.6 million for the years ended December 31, 2022 and 2021, respectively.

We do not track internal related expenses on a program-by-program basis, because our research and development employees and infrastructure resources are utilized across our development programs.

General and Administrative Expenses

Our general and administrative expenses consist primarily of salaries and related costs, including, but not limited to, payroll taxes, benefits, non-cash stock-based compensation and travel. Other general and administrative expenses include legal costs of pursuing patent protection of our intellectual property and professional service fees for auditing, tax and general legal services. We expect our general and administrative expenses to continue to increase in the future as we expand our operating activities and prepare for potential commercialization of our current and future product candidates, increase our headcount and support our operations as a public company, including increased expenses related to legal, accounting, regulatory and tax-related services associated with maintaining compliance with requirements of the Nasdaq Global Select Market and the SEC, directors and officers liability insurance premiums and investor relations activities. Allocated expenses consist of rent expenses related to our office and research and development facilities, depreciation and other allocated costs not otherwise included in research and development expenses.

Interest Income

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

Interest Expense

Interest expense consists primarily of interest expense related to our debt facility. A portion of the interest expense is non-cash expense relating to the accretion of the final payment fees and amortization of debt discount and debt issuance costs associated with the Loan Agreement (as defined below).

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table sets forth the significant components of our results of operations (in thousands):

	Year Ended December 31,		
	2022	2021	Change
Revenues:			
Collaboration and license revenues	$ 9,269	$ 46,717	$ (37,448)
Grant revenues	10,676	1,497	9,179
Total revenues	19,945	48,214	(28,269)
Operating expenses:			
Research and development	111,403	97,490	13,913
General and administrative	28,970	25,933	3,037
Total operating expenses	140,373	123,423	16,950
Loss from operations	(120,428)	(75,209)	(45,219)
Interest income	1,976	164	1,812
Interest expense	(1,235)	(37)	(1,198)
Net loss	$ (119,687)	$ (75,082)	$ (44,605)

Collaboration and License, and Grant Revenues

Collaboration and licenses revenues were $9.3 million and $46.7 million for the years ended December 31, 2022 and 2021, respectively. During the year ended December 31, 2022, we recorded $1.6 million in collaboration revenue related to the Gilead Collaboration Agreement, and $7.7 million in collaboration revenue related to the 2seventy Agreement. The amount of collaboration revenue recognized related to the 2seventy Agreement during the year ended December 31, 2022 included cumulative catch-up adjustments increasing collaboration revenue by $6.4 million due to revisions to estimated costs to complete the remaining performance obligation. During the year ended December 31, 2021, we recorded $38.6 million in license revenue and $5.1 million in collaboration revenue related to the Gilead Collaboration Agreement, and $3.0 million in collaboration revenue related to the 2seventy Agreement. Grant revenue was $10.7 million and $1.5 million for the years ended December 31, 2022 and 2021, respectively. During the years ended December 31, 2022 and 2021, we recognized $9.5 million and $1.5 million, respectively, of grant revenue from the CEPI Funding Agreement. During the year ended December 31, 2022 we recognized $1.2 million of grant revenue from the Gates Agreement. See Note 7 to our consolidated financial statements for additional information.

Research and Development Expenses

Research and development expenses were $111.4 million for the year ended December 31, 2022 compared to $97.5 million for the year ended December 31, 2021. The increase of $13.9 million for the year ended December 31, 2022 was primarily due to increases in personnel-related costs and clinical trial expenses. Personnel-related costs increased by $8.0 million, as a direct result of our increased research and development headcount. Outside services and consultants increased by $7.9 million, as a result of clinical trials and preclinical testing, including additional temporary personnel to carry out the research and development activities. Facility related costs increased by $2.7 million to accommodate our increased research and general personnel. These increases were partially offset by a decrease of $2.9 million in laboratory supplies and consumables and milestone and license payments decreased by $1.8 million primarily reflecting payments to Genevant Sciences GmbH.

General and Administrative Expenses

General and administrative expenses were $29.0 million for the year ended December 31, 2022 compared to $25.9 million for the year ended December 31, 2021. The increase of $3.0 million was primarily attributable to a $4.1 million increase in personnel-related costs as we expanded our headcount and $0.3 million in outside services for legal, finance, recruiting and other professional services to support our ongoing operations, offset by a decrease of $0.4 million of facility related costs and $1.0 million in professional services expense due to costs incurred in the Gilead Collaboration Agreement in 2021 that did not occur again in 2022.

Interest Income

Interest income was $2.0 million for the year ended December 31, 2022. Interest income was $0.2 million for the year ended December 31, 2021. The income for both years represents interest and investment income from cash, cash equivalents and marketable securities. The increase of $1.8 million was primarily due to higher interest rates in 2022 as compared to 2021.

Interest Expense

Interest expense was $1.2 million for the year ended December 31, 2022. Interest expense was negligible for the year ended December 31, 2021. The interest expense is primarily comprised of the contractual coupon interest expense, the amortization of the debt discount and issuance costs and the accretion of the final payment fee associated with the Loan Agreement (as defined below). The increase of $1.2 million from 2021 to 2022 was due to the Loan Agreement entered into in July 2022.

Comparison of the Years Ended December 31, 2021 and 2020

The following table sets forth the significant components of our results of operations (in thousands):

	Year Ended December 31,		
	2021	2020	Change
Revenues:			
Collaboration and license revenues	$ 46,717	$ 3,462	$ 43,255
Grant revenues	1,497	575	922
Total revenues	48,214	4,037	44,177
Operating expenses:			
Research and development	97,490	88,643	8,847
General and administrative	25,933	21,411	4,522
Total operating expenses	123,423	110,054	13,369
Loss from operations	(75,209)	(106,017)	30,808
Interest income	164	715	(551)
Interest expense	(37)	(12)	(25)
Net loss	$ (75,082)	$ (105,314)	$ 30,232

Discussions of year-to-year comparisons between 2021 and 2020 that are not included in this report on Form 10-K can be found in “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in Part II, Item 7 of the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2021.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have funded our operations primarily through sales of our convertible preferred stock, sales of our common stock in public offerings and under our “at-the-market” offering programs, private placements of our common stock and pre-funded warrants, proceeds from the Loan Agreement (as defined below), and our collaborations, including with the receipt of proceeds under the 2seventy Agreement and the Gilead Collaboration Agreement, and non-dilutive grants from various nonprofit organizations. As of December 31, 2022, we had cash, cash equivalents, and marketable securities of $175.9 million and an accumulated deficit of $521.1 million, as compared to cash, cash equivalents, and marketable securities of $206.3 million and an accumulated deficit of $401.4 million as of December 31, 2021. We expect that our cash, cash equivalents, and marketable securities as of December 31, 2022 will enable us to fund our current and planned operating expenses and capital expenditures for at least the next 12 months from the date of the filing of this report.

In October 2019, we filed the 2019 Shelf Registration Statement, covering the offering of up to $250.0 million of various equity and debt securities, including the sale and issuance of up to $75.0 million worth of shares of our common stock under the 2019 ATM Offering Program. Through December 31, 2022, we have received aggregate proceeds from our 2019 ATM Offering Program of $50.0 million, net of commissions and offering costs, pursuant to the issuance of 5,642,712 shares. As of December 31, 2022, there are no further amounts available for issuance under the 2019 ATM Offering Program.

In March 2022, we filed the 2022 Shelf Registration Statement, covering the offering of up to $250.0 million of various equity and debt securities, including the sale and issuance of up to $100.0 million worth of shares of our common stock under the 2022 ATM

Offering Program. As of December 31, 2022, we have received $20.1 million in gross proceeds from our 2022 ATM Offering Program and have $79.9 million available thereunder.

In April 2022, we received the second tranche payment of $2.7 million under the CEPI Funding Agreement.

In July 2022, we entered into a loan and security agreement (the "Loan Agreement") with Hercules Capital, Inc. ("Hercules") and Silicon Valley Bank ("SVB"), which provides us with a 60-month term loan facility for the Company up to $80.0 million in borrowing capacity across five potential tranches. At the closing of the Loan Agreement, we drew $20.0 million from the first tranche, and we can draw up to an additional $10.0 million through March 2023. The remaining tranches provide up to $50.0 million borrowing capacity and become available if and when we meet certain milestones set forth in the Loan Agreement. As of December 31, 2022, one milestone had been achieved, which provides the Company to draw up to $10 million through December 15, 2023. The term loan is secured by substantially all of our assets, other than intellectual property. There are no warrants associated with the Loan Agreement.

Borrowings under the Loan Agreement bear interest (i) at an annual cash rate equal to the greater of (x) the lesser of (1) the prime rate (as customarily defined) and (2) 5.50%, in either case, plus 3.15%, and (y) 7.15% and (ii) at an annual payment-in-kind rate, which may equal 2.00%. We are required to make monthly interest-only payments prior to the amortization date of January 1, 2025, subject to a potential six-month and one-year extension upon satisfaction of certain conditions. We will also be required to pay a facility charge equal to 0.50% of the principal amount of any borrowings made pursuant to the last four tranches.

All unpaid principal and accrued and unpaid interest with respect to each term loan is due and payable in full on July 19, 2027. At our option, we may prepay all or any portion of the outstanding borrowings, plus accrued and unpaid interest thereon and fees and expenses, subject to a prepayment premium ranging from zero to 2.5%, during the first three years after closing, depending on the year of such prepayment. Upon repayment of the term loan, we will be required to make a final payment fee to the lenders equal to 5.75% of the aggregate original principal amount of the loan

Beginning on April 1, 2023, so long as our market capitalization is equal to or less than $400.0 million, we are subject to a minimum liquidity requirement equal to the then outstanding balance under the Loan Agreement multiplied by 0.55 or 0.45, which multiplier depends on whether we achieve certain performance milestones. Our obligations under the Loan Agreement are subject to acceleration upon the occurrence of customary events of default, including payment default, insolvency and the occurrence of certain events having a material adverse effect, including (but not limited to) material adverse effects upon the business, operations, properties, assets or financial condition of us and our subsidiaries, taken as a whole.

In October 2022, we completed a third private placement of securities (the "Third PIPE Financing"), pursuant to which we sold an aggregate of 6,637,165 shares of common stock at a per share purchase price of $2.26 and pre-funded warrants to purchase 13,274,923 shares of common stock at a price of $2.26 per share (of which $2.2599 per share was prepaid by each purchaser). The aggregate gross cash proceeds to us for the securities sold in the Third PIPE Financing was $45.0 million, and related costs were $2.6 million.

Future Funding Requirements

We do not expect positive cash flows from operations in the foreseeable future. Historically, we have incurred operating losses as a result of ongoing efforts to develop our cancer immunotherapy candidates, including conducting ongoing research and development, clinical and preclinical studies and providing general and administrative support for these operations. We do not have any products approved for sale, and we do not expect to generate any meaningful revenue unless and until we obtain regulatory approval of and commercialize any of our current and future product candidates and/or enter into additional significant collaboration or grant agreements with third parties, and we do not know when, or if, either will occur. We expect to continue to incur net operating losses for at least the next several years and we expect the losses to increase as we advance our CORAL, GRANITE, and SLATE programs, as well as any future product candidates, through clinical development, seek regulatory approval, prepare for and, if approved, proceed to commercialization, continue our research and development efforts and invest in our manufacturing facility. We are subject to all the risks typically related to the development of new product candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. Moreover, we incur substantial costs associated with operating as a public company. We anticipate that we will need substantial additional funding in connection with our continuing operations.

Until we can generate a sufficient amount of revenue from the commercialization sources of liquidity of immunotherapy product candidates or from additional significant collaboration or license agreements with third parties, if ever, we expect to finance our future cash needs through private and public equity offerings, including our "at-the-market" offering programs, debt financings, and potential future collaboration, license and development agreements. Additional capital may not be available on reasonable terms, if 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 one or more of our current or future product candidates. If we raise additional

funds by issuing equity or convertible debt securities, it could result in dilution to our existing stockholders and increased fixed payment obligations. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term, but we may have to relinquish valuable rights to our product candidates or grant licenses on terms that are not favorable to us. Any of the foregoing could significantly harm our business, financial condition and prospects.

Since our inception, we have incurred significant losses and negative cash flows from operations. We have an accumulated deficit of $521.1 million through December 31, 2022. We expect to incur substantial additional losses in the future as we conduct and expand our research and development activities. We believe that our existing cash, cash equivalents and marketable securities will be sufficient to enable us to fund our projected operations through at least the next twelve (12) months from the date of this Annual Report on Form 10-K. We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of product candidates, we are unable to estimate the exact amount of our operating capital requirements. Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of developing our product candidates, and of conducting preclinical studies and clinical trials, including our clinical trials for GRANITE, SLATE and CORAL;
- the timing of, and the costs involved in, obtaining regulatory approvals for our oncology and infectious disease immunotherapy product candidates; in particular, any costs incurred in connection with any future regulatory requirements that may be imposed by the FDA or foreign regulatory bodies;
- the number and characteristics of any additional product candidates we develop or acquire;
- the timing and amount of any milestone, royalty or other payments we are required to make pursuant to any current or future collaboration or license agreements;
- potential delays in our ongoing clinical trials as a result of the COVID-19 pandemic;
- the cost of manufacturing our product candidates we successfully commercialize, including the cost of scaling up our internal manufacturing operations;
- the cost of building a sales force in anticipation of product commercialization;
- the cost of commercialization activities, including building a commercial infrastructure, marketing, sales and distribution costs;
- our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- any product liability or other lawsuits related to our products;
- the costs to attract, hire and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property portfolio; and
- the timing, receipt and amount of sales of any future approved products, if any.

A change in the outcome of any of these or other variables with respect to the development of any of our current and future product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we will need additional funds to meet operational needs and capital requirements associated with such operating plans.

Cash Flows

The following table sets forth a summary of the primary sources and uses of cash for each of the periods presented below (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Cash used in operating activities	$ (115,946)	$ (50,678)	$ (89,102)
Cash (used in) provided by investing activities	(12,964)	(118,553)	65,949
Cash provided by financing activities	83,098	108,760	135,801
Net (decrease) increase in cash and cash equivalents	$ (45,812)	$ (60,471)	$ 112,648

Cash Used in Operating Activities

During the year ended December 31, 2022, cash used in operating activities was $115.9 million, which consisted of net loss of $119.7 million, adjusted by non-cash charges of $28.3 million and net changes in our operating assets and liabilities of $24.5 million. The non-cash charges consisted primarily of depreciation and amortization expense of $6.6 million, stock-based compensation of $12.6 million, non-cash operating lease expense of $9.1 million and amortization of debt discount and issuance costs of $0.4 million, partially offset by amortization premiums on marketable securities of $0.4 million. The change in our operating assets and liabilities was primarily driven by decreases of $15.2 million in deferred revenue, $8.9 million in lease liability, $0.4 million in accrued research and development expenses and an increase of $7.4 million in deposits and other long term assets, partially offset by increases of $1.3 million in accrued compensation, $1.9 million in accounts payable, $3.5 million in accrued and other non-current liabilities and a decrease of $0.7 million in prepaid expenses and other current assets.

During the year ended December 31, 2021, cash used in operating activities was $50.7 million, which consisted of a net loss of $75.1 million, adjusted by non-cash charges of $25.8 million and cash used due to changes in our operating assets and liabilities of $1.4 million. The non-cash charges consisted primarily of depreciation expense of $6.3 million, stock-based compensation of $10.6 million, and non-cash operating lease expense of $8.1 million. The change in our operating assets and liabilities was primarily due to decreases of $7.9 million in lease liability, $0.9 million in accrued and other non-current liabilities, $3.4 million in prepaid expenses and other assets, $0.6 million in deposits and long-term assets and $0.4 million in accounts payable, offset by increases of $8.6 million in deferred revenue, $2.6 million in accrued research and development expenses, and $0.6 million in accrued compensation.

During the year ended December 31, 2020, cash used in operating activities was $89.1 million, which consisted of a net loss of $105.3 million, adjusted by non-cash charges of $21.1 million and cash used due to changes in our operating assets and liabilities of $4.9 million. The non-cash charges consisted primarily of depreciation and amortization expense of $6.6 million, stock-based compensation of $7.1 million, and non-cash operating lease expense of $7.5 million. The change in our operating assets and liabilities was primarily due to decreases of $3.8 million in lease liability, $2.8 million in deferred revenue, $0.7 million in accrued research and development expenses, and $0.9 million in prepaid expenses and other assets, offset by increases of $0.8 million in accounts payable, $1.7 million in accrued compensation and $0.7 million in accrued and other non-current liabilities.

Cash (Used in) Provided by Investing Activities

During the year ended December 31, 2022, cash used in investing activities was $13.0 million which consisted of $141.9 million in purchases of marketable securities and $5.9 million of capital expenditures to purchase property and equipment, offset by $134.8 million in proceeds from the maturity of marketable securities.

During the year ended December 31, 2021, cash used in investing activities was $118.6 million, which consisted of $199.9 million of purchases of marketable securities, $5.5 million of capital expenditures to purchase property and equipment, and $0.2 million of prepayment of financing lease, offset by $82.2 million in proceeds from the maturity of marketable securities and $4.8 million in proceeds from the sale of marketable securities.

During the year ended December 31, 2020, cash provided by investing activities was $65.9 million, which consisted of $72.9 million in proceeds from the maturity of marketable securities and $5.4 million in proceeds from the sale of marketable securities, offset by $8.8 million of purchases of marketable securities and $3.5 million of capital expenditures to purchase property and equipment.

Cash Provided by Financing Activities

During the year ended December 31, 2022, cash provided by financing activities was $83.1 million, which primarily consisted of $45.0 million in proceeds from the Third PIPE Financing, $19.1 million in proceeds from long-term debt, net of debt discount and issuance costs, $19.7 million in proceeds from the 2022 ATM Offering Program, $0.3 million in proceeds from the issuance of common stock from option and warrant exercises and $0.5 million in proceeds from issuance of common stock under the employee stock purchase plan, offset by $0.9 million in tax withholding on vesting of restricted stock units, $0.4 million in payment of financing costs, and $0.2 million in payment of financing lease.

During the year ended December 31, 2021, cash provided by financing activities was $108.8 million, which primarily consisted of proceeds from the issuance of common stock of $55.0 million from the second PIPE financing, $36.6 million from “at the market offering”, net of issuance costs, $21.2 million under the Gilead Stock Purchase Agreement, $3.4 million from the exercise of stock options, warrants and other, and $0.9 million from the purchase of shares under our employee stock purchase plan, offset by $8.4 million of payments of financing costs.

During the year ended December 31, 2020, cash provided by financing activities was $135.8 million, which primarily consisted of $125.0 million in proceeds from sale of common stock and pre-funded warrants to purchase shares of our common stock in a series of private placement transactions, $9.8 million in proceeds from the issuance of common stock related to our “at the market offering,” $0.9 million in proceeds from the issuance of common stock from the purchase of shares under our employee stock purchase plan, and $0.2 million in proceeds from the exercise of stock options, offset by $0.1 million of payments of financing costs.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements, as defined under SEC rules.

Contractual Obligations and Commitments

We lease office, laboratory and storage space in facilities at several locations in California and Massachusetts. The terms of our lease agreements have expiration dates between 2023 to 2033. The total future minimum lease payments under the agreements are $105.0 million, of which $8.6 million of the payments are due in the next year. See Note 6 to our consolidated financial statements.

We are party to license agreements pursuant to which we have in-licensed various intellectual property rights. The license agreements obligate us to make certain milestone payments related to achievement of specified events, as well as royalties in the low-single digits based on sales of licensed products. In August 2019, following the initial patient treatment of SLATE, we recorded $3.0 million as research and development expense in connection with the milestone. In October 2020, we made a milestone payment of $2.0 million pursuant to an option and license development agreement with Genevant. During the years ended December 31, 2022 and 2021, no royalties were due from the sales of licensed products. See Note 7 to our consolidated financial statements for additional information.

From time to time, in the normal course of business, we enter into contracts in the normal course of business with CROs for clinical trials and CMOs for clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes, which generally provide for termination within 30 days of notice, and therefore are cancelable contracts.

Critical Accounting Policies and Use of Estimates

This discussion and analysis of financial condition and results of operation is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States (U.S. GAAP). The preparation of financial statements requires management to make estimates and judgments that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities as of the date of the financial statements and the reported amounts of expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to preclinical study trial accruals, fair value of assets and liabilities, and the fair value of common stock and stock-based compensation. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

While our significant accounting policies are more fully described in the notes to our consolidated financial statements, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our consolidated financial statements and understanding and evaluating our reported financial results.

Revenue Recognition

We perform research and development under collaboration, license, grant, and clinical development agreements. Our revenue primarily consists of collaboration agreements and grant funding agreements. At contract inception, we analyze a revenue arrangement to determine the appropriate accounting under U.S. GAAP. Currently, our revenue arrangements represent customer contracts within the scope of ASC Topic 606, Revenue from Contracts with Customers (Topic 606) (ASC 606) or grant funding agreements subject to the contribution guidance in ASC Topic 958-605, Not-for-Profit Entities – Revenue Recognition (ASC 958-605), which applies to business entities that receive contributions within the scope of ASC 958-605.

For collaboration agreements, we analyze each agreement to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements that are considered to be in the scope of the collaboration guidance and that contain multiple elements, we first determine which elements of the collaboration are deemed to be within the scope of the collaboration guidance and those that are more reflective of a vendor-customer relationship and, therefore, within the scope of the revenue with contracts with customer guidance. For elements of collaboration arrangements that are accounted for pursuant to the revenue from contracts with customer guidance, an appropriate recognition method is determined and applied consistently, generally by analogy to the revenue from contracts with customers guidance.

The terms of the collaboration and license agreements entered into typically include payment of one or more of the following: non-refundable, up-front fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services; and royalties on net sales of licensed products. Each of these payments results in license, collaboration, and other revenues, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues. The core principle of the accounting for revenue from contracts with customers guidance is to recognize revenues when promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received in exchange for those goods or services.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under each of our agreements, we perform 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 constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in our consolidated balance sheets. If the related performance obligation is expected to be satisfied within the next twelve (12) months this will be classified in current liabilities. Amounts recognized as revenue prior to receipt are recorded as contract assets in our consolidated balance sheets. If we expect to have an unconditional right to receive consideration in the next twelve (12) months, this will be classified in current assets. A net contract asset or liability is presented for each contract with a customer.

At contract inception, we assess the goods or services promised in a contract with a customer and identify those distinct goods and services that represent a performance obligation. A promised good or service may not be identified as a performance obligation if it is immaterial in the context of the contract with the customer, if it is not separately identifiable from other promises in the contract (either because it is not capable of being separated or because it is not separable in the context of the contract), or if the performance obligation does not provide the customer with a material right.

We consider the terms of the contract and our customary business practices to determine the transaction price. The transaction price is the amount of consideration to which we expect to be entitled in exchange for transferring promised goods or services to a customer. The consideration promised in a contract with a customer may include fixed amounts, variable amounts, or both. Variable consideration will only be included in the transaction price when it is not considered constrained, which is when it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur.

If it is determined that multiple performance obligations exist, the transaction price is allocated at the inception of the agreement to all identified performance obligations based on the relative standalone selling prices. The relative selling price for each deliverable is estimated using objective evidence if it is available. If objective evidence is not available, we use our best estimate of the selling price for the deliverable.

Revenue is recognized when, or as, we satisfy a performance obligation by transferring a promised good or service to a customer. An asset is transferred when, or as, the customer obtains control of that asset, which for a service, is considered to be as the services are

received and used. We recognize revenue over time by measuring the progress toward complete satisfaction of the relevant performance obligation using an appropriate input or output method based on the nature of the good or service promised to the customer.

After contract inception, the transaction price is reassessed at every period end and updated for changes such as resolution of uncertain events. Any change in the transaction price is allocated to the performance obligations on the same basis as at contract inception.

Management may be required to exercise considerable judgment in estimating revenue to be recognized. Judgment is required in identifying performance obligations, estimating the transaction price, estimating the stand-alone selling prices of identified performance obligations, which may include forecasted revenue, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success, and estimating the progress towards satisfaction of performance obligations.

For grant funding agreements, grant revenue is recognized during the period that the research and development services occur, as qualifying expenses are incurred. We concluded that payments received under these grants represent nonreciprocal contributions, as described in ASC 958, Not-for-Profit Entities, and that the grants are not within the scope of ASC 606 as the organization providing the grant does not meet the definition of a customer. Grant revenue relates primarily to the CEPI Funding Agreement and the Gates Grant Agreement (see Note 7).

Research and Development Expenses

We record research and development expenses to operations as incurred. Research and development expenses represent costs incurred by us for the discovery and development of our product candidates and the development of our technology and include: internal research and development expense, including employee-related expenses (such as salaries, benefits, travel and non-cash stock-based compensation expense); external research and development expenses incurred under arrangements with third parties, such as CROs, preclinical testing organizations, contract manufacturing organizations (CMOs), academic and non-profit institutions and consultants; license fees; other expenses, which include direct and allocated expenses for laboratory, facilities and other costs; and costs incurred related to our collaboration agreements. Costs to develop our technologies are recorded as research and development expense unless the criteria to be capitalized as internal-use software costs is met.

As part of the process of preparing financial statements, we are required to estimate and accrue expenses. We record the estimated expenses of research and development activities conducted by third-party service providers based upon the estimated amount of services provided within research and development expense in the consolidated statements of operations and comprehensive loss. These services include the conduct of clinical and preclinical studies, contract manufacturing activities and consulting services. Payments made prior to the receipt of goods or services to be used in research and development are deferred and recognized as expense in the period in which the related goods are received or services are realized or consumed. If the costs have been prepaid, this expense reduces the prepaid expenses in the consolidated balance sheets, and if not yet invoiced, the costs are included in accrued liabilities in the consolidated balance sheets. These costs are a significant component of our research and development expenses. We record amortization of prepaid expenses or accrued expenses for these costs based on the estimated amount of work completed and in accordance with agreements established with these third parties. Such payments are evaluated for current or long-term classification based on when they will be realized.

Costs for certain research and development activities are recognized based on an evaluation of the progress to completion of specific tasks. We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, we adjust our accrued estimates. 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 may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from external CROs, CMOs, and other third-party service providers. To date, we have not experienced material differences between our accrued expenses and actual expenses.

Leases

We determine whether the arrangement is or contains a lease at the inception of the arrangement and if such a lease is classified as a financing lease or operating lease. The majority of the Company’s leases are classified as operating leases. Leases with a term greater than one year are recognized on the consolidated balance sheets as right-of-use assets, lease liabilities and, if applicable, long-term lease liabilities. Lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not readily determinable. As such, we

utilize the appropriate incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. We derived our incremental borrowing rate by assessing rates in recent market transactions, as adjusted for security interests and our credit quality. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received and impairment charges if we determine the right-of-use asset is impaired.

JOBS Act

We are an emerging growth company under the Jumpstart Our Business Startups Act of 2012. As an emerging growth company, we may delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have nonetheless irrevocably elected not to avail ourselves of this exemption and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We will remain an emerging growth company until the earliest of (1) December 31, 2023, (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a “large accelerated filer” as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such year or (4) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

Recent Accounting Pronouncements

Refer to “Note 2. Summary of Significant Accounting Policies” to our audited consolidated financial statements for a discussion of recent accounting pronouncements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Sensitivity

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and marketable securities of $175.9 million as of December 31, 2022, which consisted primarily of money market funds and marketable securities, largely composed of investment grade, short-term and long-term fixed income securities.

The primary objective of our investment activities is to preserve capital to fund our operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of investments in a variety of securities of high credit quality and short-term duration, according to our board-approved investment charter.

Our investments are subject to interest rate risk and could fall in value if market interest rates increase. A hypothetical 10% relative change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and our clinical trial costs. We do not believe that inflation has had a material effect on our business, results of operations, or financial condition.

Item 8. Financial Statements and Supplementary Data

Gritstone bio, Inc.

Index to Financial Statements

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of
Gritstone bio, Inc.

Opinion on the Financial Statements

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

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2016.

San Mateo, California
March 9, 2023

Gritstone bio, Inc.
Consolidated Balance Sheets

(In thousands, except share amounts and par value)

	December 31,	
	2022	2021
Assets		
Current assets:		
Cash and cash equivalents	$ 55,498	$ 93,287
Marketable securities	116,389	108,346
Restricted cash	3,977	11,285
Prepaid expenses and other current assets	7,014	7,672
Total current assets	182,878	220,590
Long-term restricted cash	5,290	6,005
Property and equipment, net	21,335	21,622
Lease right-of-use assets	17,481	22,920
Deposits and other long-term assets	9,739	2,352
Long-term marketable securities	4,031	4,617
Total assets	$ 240,754	$ 278,106
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 8,694	$ 4,230
Accrued compensation	8,215	6,925
Accrued liabilities	4,124	411
Accrued research and development expenses	3,343	3,706
Lease liabilities, current portion	5,294	7,483
Deferred revenue, current portion	5,131	17,201
Total current liabilities	34,801	39,956
Other liabilities, noncurrent	150	—
Lease liabilities, net of current portion	15,673	18,936
Deferred revenue, net of current portion	—	3,128
Debt, noncurrent	19,349	—
Total liabilities	69,973	62,020
Commitments and contingencies (Notes 6, 7, and 8)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized; no shares issued and outstanding at December 31, 2022 and 2021	—	—
Common stock, $0.0001 par value; 300,000,000 shares authorized at December 31, 2022 and 2021; 86,894,901 and 69,047,878 shares issued and outstanding at December 31, 2022 and 2021, respectively	22	20
Additional paid-in capital	691,910	617,523
Accumulated other comprehensive loss	(80)	(73)
Accumulated deficit	(521,071)	(401,384)
Total stockholders' equity	170,781	216,086
Total liabilities and stockholders' equity	$ 240,754	$ 278,106

See accompanying notes to consolidated financial statements.

Gritstone bio, Inc.
Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2022	2021	2020
Revenues:			
Collaboration and license revenues	$ 9,269	$ 46,717	$ 3,462
Grant revenues	10,676	1,497	575
Total revenues	19,945	48,214	4,037
Operating expenses:			
Research and development	111,403	97,490	88,643
General and administrative	28,970	25,933	21,411
Total operating expenses	140,373	123,423	110,054
Loss from operations	(120,428)	(75,209)	(106,017)
Interest income	1,976	164	715
Interest expense	(1,235)	(37)	(12)
Net loss	(119,687)	(75,082)	(105,314)
Other comprehensive loss:			
Unrealized loss on marketable securities	(7)	(73)	(24)
Comprehensive loss	$ (119,694)	$ (75,155)	$ (105,338)
Net loss per share, basic and diluted	$ (1.32)	$ (0.95)	$ (2.79)
Weighted-average number of shares used in computing net loss per share, basic and diluted	90,918,333	78,885,186	37,792,365

See accompanying notes to consolidated financial statements.

Gritstone bio, Inc.
Consolidated Statements of Stockholders' Equity

(In thousands, except share amounts)

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders
	Shares	Amount	Capital	Gain (Loss)	Deficit	Equity
Balance at December 31, 2019	36,332,956	17	355,291	24	(220,988)	134,344
Issuance of common stock under private investment in public equity ("PIPE") financing, net of issuance costs of $1,394	9,586,478	1	32,121	—	—	32,122
Issuance of pre-funded warrants, net of issuance costs of $3,806	—	—	87,704	—	—	87,704
Issuance of common stock under ATM equity offering program, net of issuance costs of $104	1,160,963	—	9,670	—	—	9,670
Issuance of common stock under ESPP	243,878	—	910	—	—	910
Unrealized loss on marketable securities	—	—	—	(24)	—	(24)
Lapse of repurchase rights related to common stock issued pursuant to early exercises	30,874	—	11	—	—	11
Issuance of common stock upon exercise of stock options	197,544	—	206	—	—	206
Stock-based compensation	—	—	7,110	—	—	7,110
Net loss	—	—	—	—	(105,314)	(105,314)
Balance at December 31, 2020	47,552,693	$ 18	$ 493,023	$ —	$ (326,302)	$ 166,739
Offering costs related to the sale of common stock and pre-funded warrants	—	—	(451)	—	—	(451)
Issuance of common stock under Sales Purchase Agreement, net of issuance costs of $339	1,169,591	—	20,830	—	—	20,830
Issuance of common stock under the ATM equity offering program, net of issuance costs of $124	3,990,869	—	36,595	—	—	36,595
Issuance of common stock under PIPE financing, net of issuance costs of $2,348	5,000,000	1	52,652	—	—	52,653
Issuance of common stock under the ESPP	183,111	—	914	—	—	914
Unrealized loss on marketable securities	—	—	—	(73)	—	(73)
Issuance of common stock upon exercise of warrants	10,459,576	1	48	—	—	49
Issuance of common stock upon exercise of stock options	692,038	—	3,360	—	—	3,360
Stock-based compensation	—	—	10,552	—	—	10,552
Net loss	—	—	—	—	(75,082)	(75,082)
Balance at December 31, 2021	69,047,878	$ 20	$ 617,523	$ (73)	$ (401,384)	$ 216,086
Issuance of common stock under the ATM equity offering program, net of issuance costs of $146	7,034,948	1	19,591	—	—	19,592
Issuance of common stock under PIPE financing, net of issuance costs of $880	6,637,165	1	14,120	—	—	14,121
Issuance of pre-funded warrants, under PIPE financing, net of issuance costs of $1,759	—	—	28,240	—	—	28,240
Issuance of common stock upon exercise of warrants	3,442,567	—	34	—	—	34
Issuance of common stock upon restricted stock units vesting	215,350	—	—	—	—	—
Tax payments related to shares withheld for vested restricted stock units	—	—	(890)	—	—	(890)
Issuance of common stock under the ESPP	322,646	—	549	—	—	549
Unrealized loss on marketable securities	—	—	—	(7)	—	(7)
Issuance of common stock upon exercise of stock options	194,347	—	186	—	—	186
Stock-based compensation	—	—	12,557	—	—	12,557
Net loss	—	—	—	—	(119,687)	(119,687)
Balance at December 31, 2022	86,894,901	$ 22	$ 691,910	$ (80)	$ (521,071)	$ 170,781

See accompanying notes to consolidated financial statements.

Gritstone bio, Inc.
Consolidated Statements of Cash Flows

(In thousands)

	Year Ended December 31,		
	2022	2021	2020
Operating activities			
Net loss	$ (119,687)	$ (75,082)	$ (105,314)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	6,560	6,347	6,644
Net amortization of premiums and discounts on marketable securities	(372)	817	(122)
Amortization of debt discount and issuance costs	392	—	—
Stock-based compensation	12,557	10,552	7,110
Non-cash operating lease expense	9,131	8,052	7,511
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	658	(3,426)	(852)
Deposits and other long-term assets	(7,387)	(614)	49
Accounts payable	1,879	(419)	826
Accrued compensation	1,290	593	1,731
Accrued and other non-current liabilities	3,509	(859)	662
Accrued research and development expenses	(363)	2,653	(725)
Lease liability	(8,915)	(7,925)	(3,801)
Deferred revenue	(15,198)	8,633	(2,821)
Net cash used in operating activities	(115,946)	(50,678)	(89,102)
Investing activities			
Purchase of marketable securities	(141,908)	(199,905)	(8,809)
Maturities of marketable securities	134,816	82,253	72,872
Sales of marketable securities	—	4,800	5,401
Purchase of property and equipment	(5,872)	(5,463)	(3,515)
Prepayments on financing lease	—	(238)	—
Net cash (used in) provided by investing activities	(12,964)	(118,553)	65,949
Financing activities			
Proceeds from issuance of common stock from public offering	—	21,169	—
Proceeds from issuance of common stock and pre-funded warrants from PIPE financing	45,000	55,000	—
Proceeds from issuance of common stock upon exercise of stock options, warrants and other	220	3,408	198
Proceeds from issuance of common stock from ATM equity offering program	19,737	36,719	9,770
Proceeds from issuance of common stock under the ESPP	549	914	911
Proceeds from issuance of common stock and pre-funded warrants	—	—	125,026
Proceeds from long-term debt, net of debt discount and issuance costs	19,130	—	—
Payments of financing costs	(420)	(8,394)	(104)
Payments of financing lease	(228)	(56)	—
Tax payments related to shares withheld for vested restricted stock units	(890)	—	—
Net cash provided by financing activities	83,098	108,760	135,801
Net (decrease) increase in cash, cash equivalents and restricted cash	(45,812)	(60,471)	112,648
Cash, cash equivalents and restricted cash at beginning of period	110,577	171,048	58,400
Cash, cash equivalents and restricted cash at end of period	$ 64,765	$ 110,577	$ 171,048
Supplemental disclosures of non-cash investing and financing information			
Property and equipment purchases accrued but not yet paid	$ 1,146	$ 738	$ 316
Financing costs included in accrued liabilities and accounts payable	$ 2,433	$ 69	$ 5,200
Remeasurement of operating lease right-of-use asset for lease modification	$ 1,406	$ 6,452	$ 3,174
Lease liabilities arising from obtaining right -of-use asset from new leases	$ 553	$ 109	$ —
Cash paid for interest on debt	$ 647	$ —	$ —

See accompanying notes to consolidated financial statements.

1. Organization

Description of Business

Gritstone bio, Inc. ("Gritstone" or "the Company") is a biotechnology company developing targeted immunotherapies for cancer and infectious disease. The Company was incorporated in the state of Delaware in August 2015, and is based in Emeryville, California and Cambridge, Massachusetts, with a manufacturing facility in Pleasanton, California. The Company operates in one segment.

Liquidity

The Company has incurred operating losses and has an accumulated deficit as a result of ongoing efforts to develop drug product candidates, including conducting preclinical and clinical trials and providing general and administrative support for these operations. The Company had net losses of $119.7 million, $75.1 million, and $105.3 million for the years ended December 31, 2022, 2021, and 2020, respectively. The Company used net cash of $115.9 million, $50.7 million, and $89.1 million through its operating activities for the years ended December 31, 2022, 2021, and 2020, respectively. The Company had an accumulated deficit of $521.1 million and $401.4 million as of December 31, 2022 and 2021, respectively. To date, none of the Company's product candidates have been approved for sale and therefore the Company has not generated any revenue from sales of commercial products. Management expects operating losses to continue for the foreseeable future. The Company has funded its operations to date primarily through private placements of its convertible preferred stock, the sale of common stock in public offerings, under an "at the market offering" (the "ATM Offering Program"), the private placement of common stock and pre-funded warrants, and through proceeds received from its collaboration arrangements. As of December 31, 2022, the Company had cash, cash equivalents and marketable securities of $175.9 million, which the Company believes will be sufficient to fund its planned operations for a period of at least twelve months following the filing date of this Annual Report on Form 10-K.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles ("U.S. GAAP") and the rules and regulations of the Securities and Exchange Commission (the "SEC") for reporting. The consolidated financial statements are comprised of the consolidation of the Company and its wholly-owned subsidiary. All intercompany balances and transactions have been eliminated in consolidation. The Company has no unconsolidated subsidiaries or investments accounted for under the equity method.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and judgments that affect the reported amounts of assets and liabilities and disclosures of contingent liabilities as of the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Such estimates include, but are not limited to, determining the fair value of assets and liabilities, the fair value of right-of-use assets and lease liabilities, stock-based compensation expense, and transaction price and progress toward completion of performance obligation under the contracts with customers. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Fair Value of Financial Instruments

U.S. GAAP establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company.

Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

Fair value is established as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, an established three-tier fair value hierarchy distinguishes between the following:

- Level 1 inputs are quoted prices in active markets that are accessible at the market date for identical assets or liabilities.
- Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.
- Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the assets or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value instrument.

The carrying amounts reflected on the consolidated balance sheets for cash and cash equivalents, prepaid expenses and other current assets, accounts payable, accrued compensation and accrued liabilities approximate their fair values due to their short-term nature.

Cash, Cash Equivalents and Restricted Cash

Cash equivalents, which consist primarily of highly liquid investments with original maturities of three (3) months or less when purchased, are stated at fair value. These assets include investments in money market funds that invest in U.S. Treasury obligations and certificates of deposit, which are stated at fair value.

The Company has issued letters of credit under certain lease agreements that have been collateralized by cash deposits for an equal amount and are recorded within short-term restricted cash and deposits and other long-term assets on the consolidated balance sheets based on the term of the underlying lease. Additionally, the Company's restricted cash includes payments received under the Coalition for Epidemic Preparedness Innovations ("CEPI") Funding Agreement, dated as of August 14, 2021 (the "CEPI Funding Agreement") and the Gates Foundation Grant Agreement (see Note 7). The Company will utilize the CEPI and Gates Foundation funds as it incurs expenses for services performed under the agreements.

The following table provides a reconciliation of cash, cash equivalents and short-term and long-term restricted cash reported within the consolidated balance sheets that sum to the total of the same amounts shown in the consolidated statements of cash flows (in thousands):

	December 31,	
	2022	2021
Cash and cash equivalents	$ 55,498	$ 93,287
Restricted cash	3,977	11,285
Long-term restricted cash	5,290	6,005
Total cash, cash equivalents and restricted cash	$ 64,765	$ 110,577

Marketable Securities

The Company invests its excess cash in investment grade short-term and long-term fixed income securities. Such investments in marketable securities are considered available for sale, and reported at fair value, with unrealized gains and losses included as a component of accumulated other comprehensive income (loss). Marketable securities with maturities of greater than three (3) months from the date of purchase but less than one year from the consolidated balance sheet date are classified as short-term, while marketable securities with maturities in one year or beyond one year from the consolidated balance sheet date are classified as long term. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in

interest income on the consolidated statements of operations and comprehensive loss. Realized gains and losses and declines in value judged to be other than temporary, if any, on available-for-sale securities are included in interest income, net. The cost of securities sold is determined using specific identification method.

The Company periodically evaluates whether declines in fair values of its marketable securities below their book value are other than temporary. This evaluation consists of several qualitative and quantitative factors regarding the severity and duration of the unrealized loss as well as the Company's ability and intent to hold the marketable security until a forecasted recovery occurs. Additionally, the Company assesses whether it has plans to sell the security or it is more likely than not it will be required to sell any marketable securities before recovery of its amortized cost basis. Factors considered include quoted market prices, recent financial results and operating trends, implied values from any recent transactions or offers of investee securities, credit quality of debt instrument issuers, other publicly available information that may affect the value of the marketable security, duration and severity of the decline in value, and the Company's strategy and intentions for holding the marketable security. To date, the Company has not recorded any impairment charges on its marketable securities related to other-than-temporary declines in market value. No significant facts or circumstances have arisen to indicate that there has been any significant deterioration in the creditworthiness of the issuers of the securities held by us, thus there has been no recognition of any other-than-temporary impairment in the year ended December 31, 2022, 2021 or 2020. Additionally, the Company has determined that it has the ability and intent to hold all marketable securities that have been in a continuous loss position until maturity or recovery, thus there has been no recognition of any other-than-temporary impairment in the year ended December 31, 2022 or 2021.

Debt Issuance Costs and Debt Discounts

Debt issuance costs include legal fees, accounting fees, and other direct costs incurred in connection with the execution of the Company's debt financing. Debt discounts represent costs paid to the lenders. Debt issuance costs and debt discounts are deducted from the carrying amount of the debt liability and are amortized to interest expense over the term of the related debt using the effective interest method.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist of cash, cash equivalents and marketable securities. Cash, cash equivalents and marketable securities are invested through banks and other financial institutions in the United States. Such deposits may be in excess of federally insured limits. The Company maintains cash equivalents and marketable securities with various high-credit-quality and capitalized financial institutions. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds.

The Company's investment policy limits investments to certain types of securities issued by the U.S. government, its agencies, and institutions with investment-grade credit ratings and places restrictions on maturities and concentration by type and issuer. The Company is exposed to credit risk in the event of a default by the financial institutions holding its cash, cash equivalents and marketable securities and issuers of marketable securities to the extent recorded on the consolidated balance sheets. As of December 31, 2022, the Company has no off-balance sheet concentrations of credit risk.

Other Risks and Uncertainties

The Company is subject to a number of risks similar to those of other clinical-stage biotechnology companies, including dependence on key individuals; the need to develop commercially viable therapeutics; competition from other companies, many of which are larger and better capitalized; and the need to obtain adequate additional financing to fund the development of its products. The Company currently depends on third-party suppliers for key materials and services used in its research and development manufacturing process and is subject to certain risks related to the loss of these third-party suppliers or their inability to supply the Company with adequate materials and services. Further, the Company is subject to broad market risks and uncertainties resulting from recent events, such as the COVID-19 pandemic, the Russian invasion of Ukraine, inflation, rising interest rates, and recession risks as well as supply chain and labor shortages.

Property and Equipment, Net

Property and equipment are stated at cost, less accumulated depreciation and amortization. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred.

Depreciation is calculated using the straight-line method over the estimated useful lives of the respective assets, which are as follows:

Asset	Estimated Useful Life
Computer equipment and software	3 to 5 years
Furniture and fixtures	5 years
Laboratory equipment	5 to 7 years
Leasehold improvements	Shorter of useful life or lease term

Long-Lived Assets

The Company evaluates long-lived assets, including property and equipment and ROU assets, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the asset may not be fully recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. Impairment, if any, is measured as the amount by which the carrying amount of a long-lived asset exceeds its fair value. There were no indicators of impairment of long-lived assets and no impairment losses have been recorded as of and for the year ended December 31, 2022, 2021, or 2020.

Revenue Recognition

The Company performs research and development under collaboration, license, grant, and clinical development agreements. The Company's revenue primarily consists of collaboration agreements and grant funding agreements. At contract inception, the Company analyzes a revenue arrangement to determine the appropriate accounting under U.S. GAAP. Currently, the Company's revenue arrangements represent customer contracts within the scope of ASC Topic 606, Revenue from Contracts with Customers (Topic 606) ("ASC 606") or grant funding agreements subject to the contribution guidance in ASC Topic 958-605, Not-for-Profit Entities – Revenue Recognition ("ASC 958-605"), which applies to business entities that receive contributions within the scope of ASC 958-605.

For collaboration agreements, the Company analyzes to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements that are considered to be in the scope of the collaboration guidance and that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of the collaboration guidance and those that are more reflective of a vendor-customer relationship and, therefore, within the scope of the revenue with contracts with customers guidance. Elements of collaboration arrangements that are reflective of a vendor-customer relationship are accounted for pursuant to the revenue from contracts with customers guidance. The terms of the licensing and collaboration agreements entered into typically include payment of one or more of the following: non-refundable, up-front fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services; and royalties on net sales of licensed products. Each of these payments results in license, collaboration and other revenues, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues. The core principle of the accounting for revenue from contracts with customers guidance is to recognize revenues when promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received in exchange for those goods or services.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its agreements, 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 constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in the Company's consolidated balance sheets. If the related performance obligation is expected to be satisfied within the next twelve (12) months, this will be classified in current liabilities. Amounts recognized as revenue prior to receipt are recorded as contract assets in the Company's consolidated balance sheets. If the Company expects to have an unconditional right to receive consideration in the next twelve (12) months, this will be classified in current assets. A net contract asset or liability is presented for each contract with a customer.

At contract inception, the Company assesses the goods or services promised in a contract with a customer and identifies those distinct goods and services that represent a performance obligation. A promised good or service may not be identified as a performance obligation if it is immaterial in the context of the contract with the customer, if it is not separately identifiable from other promises in the contract (either because it is not capable of being separated or because it is not separable in the context of the contract), or if the performance obligation does not provide the customer with a material right.

The Company considers the terms of the contract and its customary business practices to determine the transaction price. The transaction price is the amount of consideration to which the Company expects to be entitled in exchange for transferring promised goods or services to a customer. The consideration promised in a contract with a customer may include fixed amounts, variable amounts, or both. Variable consideration will only be included in the transaction price when it is not considered constrained, which is when it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur.

If it is determined that multiple performance obligations exist, the transaction price is allocated at the inception of the agreement to all identified performance obligations, based on the relative standalone selling prices. The relative selling price for each performance obligation is estimated using objective evidence if it is available. If objective evidence is not available, the Company uses its best estimate of the selling price for the performance obligation.

Revenue is recognized when, or as, the Company satisfies a performance obligation by transferring a promised good or service to a customer. An asset is transferred when, or as, the customer obtains control of that asset, which for a service is considered to be as the services are received and used. The Company recognizes revenue over time by measuring the progress toward complete satisfaction of the relevant performance obligation, using an appropriate input or output method based on the nature of the good or service promised to the customer.

After contract inception, the transaction price is reassessed at every period end and updated for changes, such as resolution of uncertain events. Any change in the transaction price is allocated to the performance obligations on the same basis as at contract inception.

Management may be required to exercise considerable judgment in estimating revenue to be recognized. Judgment is required in identifying performance obligations, estimating the transaction price, estimating the stand-alone selling prices of identified performance obligations (which may include forecasted revenue, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success) and estimating the progress towards satisfaction of performance obligations.

For grant funding agreements, grant revenue is recognized during the period that the research and development services occur, as qualifying expenses are incurred. The Company concluded that payments received under these grants represent nonreciprocal contributions, as described in ASC 958, Not-for-Profit Entities, and that the grants are not within the scope of ASC 606 as the organization providing the grant does not meet the definition of a customer. Grant revenue relates primarily to the CEPI Funding Agreement and the Gates Grant Agreement (see Note 7).

Stock-Based Compensation

The Company measures and recognizes compensation expense for all stock-based awards made to employees, directors, and non-employees based on the grant date estimated fair value of each award. Such expense is recognized on a straight-line basis over the requisite service period which is generally the vesting period for the entire award. Expense is adjusted for estimated forfeitures. Forfeitures of awards are estimated based on historical forfeiture experience and the experience of other companies in the same industry. The estimate of forfeitures will be adjusted over the service period to the extent that actual forfeitures differ, or are expected to differ, from prior estimates.

The Company estimates the fair value of stock option grants and ESPP purchase rights using the Black-Scholes option-pricing model (“the Black-Scholes model”). The Black-Scholes model requires management to make assumptions and judgments about the variables used in the calculation, including the expected term (weighted-average period of time that the options granted are expected to be outstanding), the expected volatility of common stock, an assumed risk-free interest rate, and expected dividends the Company may pay. Management uses the simplified calculation (based on the mid-point between the vesting date and the end of the contractual term) of the expected term for its stock options as the Company has concluded that its stock option history does not provide a reasonable basis upon which to estimate expected term. Volatility is based on an average of the historical volatilities of the common stock of entities with

characteristics similar to the Company's. The risk-free rate is based on the U.S. Treasury yield curve in effect at the time of grant for periods corresponding with the expected life of the option. The Company uses an assumed dividend yield of zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock.

Research and Development Expenses

All research and development costs, including work performed by third parties, are expensed as incurred. Research and development costs consist of salaries and other personnel-related expenses, including associated non-cash stock-based compensation, consulting fees, laboratory supplies, and facility costs, as well as external research and development expenses incurred under arrangements with third parties, fees paid to other entities that conduct certain research and development activities on behalf of the Company, and costs incurred related to our collaboration agreements. Costs to develop the Company's technologies are recorded as research and development expense unless certain costs which meet the criteria to be capitalized as internal-use software costs is met. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods are received or services are realized or consumed. Such payments are evaluated for current or long-term classification based on when they will be realized.

Clinical and pre-clinical costs are a component of research and development expense. The Company accrues and expenses clinical and pre-clinical trial activities performed by third parties based upon actual work completed in accordance with agreements established with its service providers. The Company determines the actual costs through discussions with internal personnel and external service providers as to the progress or stage of completion of services and the agreed-upon fee to be paid for such services.

Leases

The Company determines whether the arrangement is or contains a lease at the inception of the arrangement and if such a lease is classified as a financing lease or operating lease. The majority of the Company's leases are classified as operating leases. Leases with a term greater than one year are included in operating lease ROU Assets, lease liabilities, current portion, and lease liabilities, net of current portion in the Company's consolidated balance sheets at December 31, 2022 and 2021. The Company has elected not to recognize on the consolidated balance sheets leases with terms of one year or less. Lease liabilities and their corresponding ROU Assets are recorded based on the present value of lease payments over the expected lease term. In determining the net present value of lease payments, the interest rate implicit in lease contracts is typically not readily determinable. As such, the Company estimates the appropriate incremental borrowing rate, which is the rate that would be incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. Certain adjustments to the ROU Assets may be required for items such as initial direct costs paid or incentives received and impairment charges if we determine the ROU Asset is impaired.

The Company considers a lease term to be the non-cancelable period that it has the right to use the underlying asset, including any periods where it is reasonably assured the Company will exercise the option to extend the contract. Periods covered by an option to extend are included in the lease term if the lessor controls the exercise of that option.

The Company recognizes lease expense on a straight-line basis over the expected lease term.

The Company has elected not to separate lease and non-lease components for its leased assets and accounts for all lease and non-lease components of its agreements as a single lease component. The lease components resulting in a ROU Asset have been recorded on the consolidated balance sheets and amortized as lease expense on a straight-line basis over the lease term.

Income Taxes

The Company accounts for income taxes under the liability method. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates that will be in effect when the differences are expected to reverse. Valuation allowances are established when necessary to reduce deferred tax assets to the amounts expected to be realized.

The Company recognizes and measures uncertain tax positions using a two—step approach set forth in authoritative guidance. The first step is to evaluate the tax position taken or expected to be taken by determining whether the weight of available evidence indicates that it is more likely than not that the tax position will be sustained in an audit, including resolution of any related appeals or litigation processes. The second step is to measure the tax benefit as the largest amount that is more than 50% likely to be realized upon ultimate settlement. Significant judgment is required to evaluate uncertain tax positions. The Company evaluates uncertain tax positions on a regular basis. The evaluations are based on a number of factors, including changes in facts and circumstances, changes in tax law, correspondence with tax authorities during the course of the audit, and effective settlement of audit issues. The provision for income taxes includes the effects of any accruals that the Company believes are appropriate. It is the Company's policy to recognize interest and penalties related to income tax matters in income tax expense. Through December 31, 2022, the Company had not accrued interest or penalties related to uncertain tax positions.

On March 18, 2020, the Families First Coronavirus Response Act (the "FFCR Act"), and on March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act") were each enacted in response to the COVID-19 pandemic. The FFCR Act and the CARES Act contain numerous income tax provisions relating to refundable payroll tax credits, deferment of employer side social security payments, net operating loss carryback periods, alternative minimum tax credit refunds, modifications to the net interest deduction limitations and technical corrections to tax depreciation methods for qualified improvement property.

On June 29, 2020, Assembly Bill 85 ("A.B. 85") was signed into California law. A.B. 85 provides for a three-year suspension of the use of net operating losses for medium and large businesses and a three-year cap on the use of business incentive tax credits to offset no more than $5.0 million of tax per year. A.B. 85 suspends the use of net operating losses for taxable years 2020 and 2021 for certain taxpayers with taxable income of $1.0 million or more. The carryover period for any net operating losses that are suspended under this provision will be extended. A.B. 85 also requires that business incentive tax credits, including carryovers, may not reduce the applicable tax by more than $5.0 million for taxable years 2020 and 2021.

The FFCR Act, CARES Act and A.B. 85 did not have a material impact on the Company's consolidated financial statements as of December 31, 2022.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' equity that are excluded from net loss, primarily unrealized gains and losses on the Company's marketable securities.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given the net loss for each period presented.

Recently Adopted Accounting Pronouncements

In October 2020, the FASB issued ASU No. 2020-10, *Codification Improvements* ("ASU 2020-10"). The standard contains improvements to the FASB Accounting Standards Codification (the "Codification") by ensuring that all guidance that requires or provides an option for an entity to provide information in the notes to financial statements is codified in the disclosure section of the Codification. The standard also improves various topics in the Codification so that entities can apply guidance more consistently on codifications that are varied in nature where the original guidance may have been unclear. The amendments in ASU 2020-10 are effective for the Company for fiscal years beginning after December 15, 2021, and interim periods within fiscal years beginning after December 15, 2022. Early adoption is permitted. We adopted ASU 2020-10 on January 1, 2022 and the adoption did not have a material impact on the Company's consolidated financial statements and related disclosures.

Recently Issued Accounting Pronouncements Not Yet Adopted

In August 2020, the FASB issued ASU No. 2020-06, *Debt - Debt with Conversion and Other Options* (Subtopic 470-20) and *Derivatives and Hedging - Contracts in Entity's Own Equity* ("ASU 2020-06"). The standard eliminates the beneficial conversion and cash conversion accounting models for convertible instruments. It also amends the accounting for certain contracts in an entity's own equity that are currently accounted for as derivatives because of specific settlement provisions. In addition, the standard modifies how

particular convertible instruments and certain contracts that may be settled in cash or shares impact the diluted EPS computation. The amendments in ASU 2020-06 are effective for the Company as defined by the SEC for fiscal years beginning after December 15, 2023, including interim periods within those fiscal years. Early adoption is permitted, but not earlier than fiscal years beginning after December 15, 2020. The Company does not expect the adoption of ASU 2020-06 to have a material impact on its consolidated financial statements and related disclosures.

3. Cash Equivalents and Marketable Securities

The amortized cost, unrealized gains and losses and fair values of cash equivalents and marketable securities were as follows (in thousands):

	December 31, 2022			
Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 38,191	$ —	$ —	$ 38,191
Total cash equivalents	38,191	—	—	38,191
Short-term marketable securities:				
Certificates of deposit	948	1	—	949
Commercial paper	33,318	23	(13)	33,328
Corporate debt securities	21,887	6	(40)	21,853
U.S. treasuries	35,608	3	(71)	35,540
U.S. government debt securities	24,703	22	(6)	24,719
Total short-term marketable securities	116,464	55	(130)	116,389
Long-term marketable securities:				
Corporate debt securities	933	—	(1)	932
U.S. treasuries	3,103	—	(4)	3,099
Total long-term marketable securities	4,036	—	(5)	4,031
Total	$ 158,691	$ 55	$ (135)	$ 158,611

	December 31, 2021			
Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 79,281	$ —	$ —	$ 79,281
Commercial paper	1,000	—	—	1,000
Corporate debt securities	1,031	—	—	1,031
Total cash equivalents	81,312	—	—	81,312
Short-term marketable securities:				
Certificates of deposit	5,600	—	(6)	5,594
Commercial paper	44,990	—	(16)	44,974
Corporate debt securities	26,976	—	(23)	26,953
U.S. treasuries	12,277	—	(8)	12,269
U.S. government debt securities	2,000	—	(1)	1,999
Asset backed securities	16,565	—	(8)	16,557
Total short-term marketable securities	108,408	—	(62)	108,346
Long-term marketable securities:				
Corporate debt securities	1,637	—	(6)	1,631
U.S. treasuries	2,991	—	(5)	2,986
Total long-term marketable securities	4,628	—	(11)	4,617
Total	$ 194,348	$ —	$ (73)	$ 194,275

As of December 31, 2022 and 2021, the Company had a total of $175.9 million and $206.3 million in cash, cash equivalents and marketable securities, which includes $55.5 million and $93.3 million in cash and cash equivalents and $120.4 million and $113.0 million in marketable securities, respectively.

All marketable securities held as of December 31, 2022, had contractual effective maturities of less than two years. There have been no material realized gains or losses on marketable securities for the periods presented. As of December 31, 2022, the Company did not hold any individual securities in an unrealized loss position for 12 months or greater. The Company has the ability and intent to hold all marketable securities that have been in a continuous loss position until maturity or recovery. No significant facts or circumstances have arisen to indicate that there has been any significant deterioration in the creditworthiness of the issuers of the securities held by us, thus there has been no recognition of any other-than-temporary impairment in the year ended December 31, 2022, 2021, or 2020. The Company has not recorded an allowance for credit losses as of December 31, 2022 or 2021.

See Note 4 for further information regarding the fair value of the Company's financial instruments.

4. Fair Value Measurements

The Company's financial assets and liabilities subject to fair value measurements on a recurring basis and the level of inputs used in such measurements were as follows (in thousands):

	December 31, 2022			
Description	**Total**	**Level 1**	**Level 2**	**Level 3**
Cash equivalents:				
Money market funds	$ 38,191	$ 38,191	$ —	$ —
Total cash equivalents	38,191	38,191	—	—
Short-term marketable securities:				
Certificates of deposit	949	—	949	—
Commercial paper	33,328	—	33,328	—
Corporate debt securities	21,853	—	21,853	—
U.S. treasuries	35,540	35,540	—	—
U.S. government debt securities	24,719	—	24,719	—
Total short-term marketable securities	116,389	35,540	80,849	—
Long-term marketable securities:				
Corporate debt securities	932	—	932	—
U.S. treasuries	3,099	3,099	—	—
Total long-term marketable securities	4,031	3,099	932	—
Total	$ 158,611	$ 76,830	$ 81,781	$ —

Description	December 31, 2021			
	Total	Level 1	Level 2	Level 3
Cash equivalents:				
Money market funds	$ 79,281	$ 79,281	$ —	$ —
Commercial paper	1,000	—	1,000	—
Corporate debt securities	1,031	—	1,031	—
Total cash equivalents	81,312	79,281	2,031	—
Short-term marketable securities:				
Certificates of deposit	5,594	—	5,594	—
Commercial paper	44,974	—	44,974	—
Corporate debt securities	26,953	—	26,953	—
U.S. treasuries	12,269	12,269	—	—
U.S. government debt securities	1,999	—	1,999	—
Asset backed securities	16,557	—	16,557	—
Total short-term marketable securities	108,346	12,269	96,077	—
Long-term marketable securities:				
Corporate debt securities	1,631	—	1,631	—
U.S. treasuries	2,986	2,986	—	—
Total long-term marketable securities	4,617	2,986	1,631	—
Total	$ 194,275	$ 94,536	$ 99,739	$ —

The Company measures the fair value of money market funds and U.S. treasuries based on quoted prices in active markets for identical securities. Commercial paper, corporate debt securities, certificates of deposits, asset backed securities, and U.S. government debt securities are valued taking into consideration valuations obtained from third-party pricing services. These pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of, and broker/dealer quotes on, the same or similar securities, issuer credit spreads; benchmark securities; prepayment/default projections based on historical data; and other observable inputs.

There were no transfers between Level 1 and Level 2 during the periods presented. See Note 3 for further information regarding the amortized cost of our financial instruments.

5. Property and Equipment, Net

Property and equipment and related accumulated depreciation and amortization are as follows (in thousands):

	December 31,	
	2022	2021
Computer equipment and software	$ 1,155	$ 987
Furniture and fixtures	2,285	2,113
Laboratory equipment	27,309	24,679
Leasehold improvements	18,024	14,128
	48,773	41,907
Less accumulated depreciation and amortization	(28,782)	(22,276)
Construction-in-progress	1,344	1,991
Total property and equipment, net	$ 21,335	$ 21,622

Depreciation and amortization expense was $6.6 million, $6.3 million, and $6.6 million for the years ended December 31, 2022, 2021, and 2020, respectively.

6. Commitments and Contingencies

Leases

The Company leases office, laboratory and storage space in facilities at several locations:

Emeryville Lease

The Company's principal executive offices in Emeryville, California, consisting of office and laboratory space, are leased pursuant to a 120-month operating lease (the "Emeryville Lease"), which the Company entered into in January 2019, with the obligation to pay rent commencing in November 2019. In conjunction with signing the Emeryville Lease, the Company paid a cash security deposit of $0.6 million, which is recorded as a deposit on the Company's consolidated balance sheets as of December 31, 2022 and 2021. The Emeryville Lease includes a free rent period, an escalation clause for increased rent and a renewal provision allowing the Company to extend this lease for an additional two five-year periods at the then market rental rate. The lessor provided the Company a tenant improvement allowance for a total of $4.0 million to complete the laboratory and office renovation. The Company has determined the tenant improvements to be lessee owned and therefore has recorded a $8.1 million ROU Asset and a $12.8 million lease liability on the consolidated balance sheet as of December 31, 2022. The Company recorded a $8.7 million ROU Asset and a $13.9 million lease liability on the consolidated balance sheet as of December 31, 2021.

Pleasanton Leases

The Company leases 42,620 square feet of office, cleanroom, and laboratory support manufacturing space in Pleasanton, California pursuant to a non-cancelable operating lease (the "Pleasanton Lease"), which the Company entered into in March 2017, with the obligation to pay rent commencing in December 2017. The Pleasanton Lease includes a free rent period, escalating rent payments and a term that expires on November 30, 2024. The Company may extend the lease term for a period of five years at the then market rental rate. The Company obtained an irrevocable letter of credit in March 2017 in the initial amount of approximately $1.0 million as a security deposit to the Pleasanton Lease, which may be drawn down by the landlord in the event the Company fails to fully and faithfully perform its obligations under the Pleasanton lease. The letter of credit may be reduced based on certain levels of cash and cash equivalents the Company holds. In October 2022, the letter of credit was reduced to a balance of $0.6 million. As of December 31, 2022, none of the irrevocable letter of credit amount had been drawn. The Pleasanton Lease further provides that the Company is obligated to pay to the landlord its proportionate share of certain basic operating costs, including taxes and operating expenses.

In connection with the Pleasanton Lease, the Company received a tenant improvement allowance of $1.2 million from the landlord for the costs associated with the design, development and construction of tenant improvements. The unamortized tenant improvement balance is recognized as a component of operating lease ROU Assets on the consolidated balance sheets as of December 31, 2022 and 2021.

In addition, in May 2019, the Company entered into a 64-month non-cancelable operating lease for additional office space in Pleasanton, California, with an obligation to pay rent commencing in August 2019. In January 2022, the Company amended the lease to add additional leased space and extend the lease expiration date to February 2027.

Cambridge Leases

The Company leases laboratory, office and storage space in several facilities in Cambridge, Massachusetts, pursuant to three separate agreements:

The Company's facility located at 40 Erie Street in Cambridge, Massachusetts is leased pursuant to a 67-month non-cancelable operating lease (the "40 Erie Lease"), which the Company entered into in February 2016, with an obligation to pay rent commencing in October 2016. The lessor provided the Company a tenant improvement allowance for a total of $2.1 million to complete the laboratory and office renovation. In September 2021, the Company executed an amendment to the 40 Erie Lease, which extends its term through April 2025 and provides for monthly base rent amounts, subject to annual increases over the term of the lease.

The Company's facility located at 21 Erie Street in Cambridge, Massachusetts is leased pursuant to a 24-month non-cancelable operating lease (the "21 Erie Lease"), which the Company entered into in September 2018. The 21 Erie Lease has since been amended five times, as a result of which the lease term extends through June 2023.

In March 2021, the Company entered into a 17-month operating lease (the "Cambridge Storage Lease") for additional office and laboratory storage space in Cambridge, Massachusetts, which commenced on April 1, 2021. The Company also paid an insignificant cash security deposit. The Cambridge Storage Lease was amended in June 2022 to extend the lease term through June 30, 2023.

In conjunction with the 40 Erie Lease, the 21 Erie Lease and the Cambridge Storage Lease, each as amended (if applicable), the Company has paid certain cash security deposits, which in each case included amounts for the applicable last month's rent and has been classified as part of the operating lease ROU Assets. Of the $0.7 million security deposits, $0.4 million was recorded in prepaids and other assets on the Company's consolidated balance sheet and the remaining $0.3 million was recorded in deposits and other long-term assets on the Company's consolidated balance sheet as of December 31, 2022. Security deposits of $0.7 million are recorded in deposits and other long-term assets on the Company's consolidated balance sheet as of December 31, 2021.

Boston Lease

The Company plans to occupy a newly-built facility in Boston, Massachusetts, with office and laboratory space, in 2023 pursuant to a 120-month operating lease (the "Boston Lease"), which the Company entered into in September 2021. The Boston Lease includes a free rent period, an escalation clause for increased rent and a renewal provision allowing the Company to extend the Boston Lease for two additional five-year periods at the then market rental rate. The landlord provided the Company with a tenant improvement allowance of up to approximately $19.1 million for costs relating to the design, permitting and construction of improvements. The Company's obligation to pay rent is expected to commence in the second half of 2023, subject to free rent periods of three and six months with respect to certain premises. The Company expects to be provided early access to the premises to install fixtures and equipment 60 days prior to the anticipated rent commencement date. The Boston Lease is expected to expire in 2033. The Boston Lease further provides that the Company is obligated to pay to the landlord its proportionate share of certain basic operating costs, including taxes and operating expenses. In connection with the Boston Lease and as a security deposit thereunder, the Company has provided the landlord an irrevocable letter of credit in the amount of approximately $4.6 million, which is collateralized by a restricted cash deposit of $4.7 million, and which may be reduced in the fifth and seventh years of the Boston Lease. As of December 31, 2022, none of the irrevocable letter of credit amount had been drawn.

The Company has not recognized a right-of-use asset or lease liability as of December 31, 2022 or 2021 for the Boston Lease as the Company did not control the underlying assets at any time in the periods ended December 31, 2022 or 2021. Under the Boston Lease, the Company is obligated to make minimum lease payments of approximately $79.1 million for the years from 2023 to 2033, which includes rent abatement during the free rent periods.

The Company's operating leases include various covenants, indemnities, defaults, termination rights, security deposits and other provisions customary for lease transactions of this nature.

The components of lease costs, which were included in our consolidated statements of operations and comprehensive loss, were as follows (in thousands):

	Year ended December 31,		
	2022	2021	2020
Lease cost			
Operating lease cost	$ 8,797	$ 7,973	$ 7,511
Short-term lease cost	—	—	7
Total lease cost	$ 8,797	$ 7,973	$ 7,518

Supplemental information related to leases was as follows:

	Year ended December 31,		
	2022	2021	2020
Cash paid for amounts included in the measurement of lease liabilities (in thousands):			
Operating cash flows from operating leases	$ 8,915	$ 7,925	$ 5,389
New right-of-use assets obtained in exchange for lease obligations (in thousands):			
Operating leases	$ 1,959	$ 6,562	$ 3,174
Weighted average remaining lease term (years):			
Operating leases	5.10	5.30	6.10
Weighted average discount rate:			
Operating leases	7.7%	7.4%	9.0%

As of December 31, 2022, minimum annual payments under the Company's lease agreements are as follows (in thousands):

	Lease Financing Obligation
Year ending December 31,	
2023	8,604
2024	12,527
2025	10,658
2026	10,376
2027	10,466
Thereafter	52,348
Total minimum payments	104,979
Less: Amounts representing interest expense	(4,899)
Less: Amounts representing lease payments under Boston lease	(79,113)
Present value of future minimum lease payments	20,967
Less: Current portion of lease liability	(5,294)
Noncurrent portion of lease liability	$ 15,673

Guarantees and Indemnifications

The Company, as permitted under Delaware law and in accordance with its certificate of incorporation and bylaws, and pursuant to indemnification agreements with certain of its officers and directors, indemnifies its officers and directors for certain events or occurrences, subject to certain limits, with respect to which the officer or director is or was serving at the Company's request in such capacity. The term of the indemnification period lasts as long as an officer or director may be subject to any proceeding arising out of acts or omissions of such officer or director in such capacity. The maximum amount of potential future indemnification is unlimited; however, the Company currently holds director and officer liability insurance. This insurance limits the Company's exposure and may enable it to recover a portion of any future amounts paid. The Company believes that the fair value of these indemnification obligations is minimal. Accordingly, the Company has not recognized any liabilities relating to these obligations for any period presented.

7. Collaboration and License Agreements

2seventy bio, Inc.

In August 2018, the Company entered into a Research Collaboration and License Agreement with bluebird bio, Inc. ("bluebird"). In November 2021, bluebird assigned the Research Collaboration and License Agreement (the "2seventy Agreement"), to its affiliate, 2seventy bio, Inc. ("2seventy"), in connection with an internal restructuring and subsequent spin-out of 2seventy. Under the terms of the 2seventy Agreement, the Company provides to 2seventy tumor-specific targets across several tumor types and, in certain cases, T cell receptors (TCR) directed to those targets. The Company received a non-refundable upfront payment of $20.0 million, and 2seventy also concurrently acquired 768,115 shares of the Company's Series C convertible preferred stock for $10.0 million at $13.04 per share. Per the 2seventy Agreement, 2seventy was also provided an option to acquire shares of the Company's common stock at the same price

as all other investors in connection with the Company's initial public offering ("IPO"). In October 2018, 2seventy purchased 666,667 shares of the Company's common stock at the price to the public of $15.00 per share for a total of $10.0 million. Under the terms of the 2seventy Agreement, the Company is eligible to earn development, regulatory, and sales-based milestones in an amount of up to $1.2 billion, and single-digit royalties on sales of products that utilize the technology subject to the 2seventy Agreement. None of these events had occurred as of December 31, 2022, and no royalties were due from the sale of licensed products.

In August 2019, the Company entered into a First Amendment to the 2seventy Agreement, which extended the timeline for the Company and 2seventy to execute a Patient Selection Services Agreement from within one year to within two years after the Effective Date of the 2seventy Agreement. In August 2020, the Company entered into a Second Amendment, which extended the timeline of the Patient Selection Services Agreement to within three years and also extended the Tissue Analysis Period from February 28, 2021 to June 30, 2021. In April 2021, the Company entered into a Third Amendment, which removed the Patient Selection Services Agreement in its entirety and extended the Tissue Analysis Period from June 30, 2021 to December 31, 2021. The amendments were entered into for administrative purposes, and the Company determined the amendments were not a modification of contract under the contract with customers guidance.

2seventy may terminate the 2seventy Agreement by giving a 120-day prior written notice to the Company at any time after the effective date of the agreement. Unless terminated early, the agreement has a term that ends upon the last payment owed by the Company on a licensed product. The 2seventy Agreement may be terminated for cause by either party based on an uncured material breach by the other party or bankruptcy of the other party. Upon early termination, all ongoing activities under the agreement and all mutual collaboration, development and commercialization licenses and sublicenses will terminate. The licenses granted by the Company to 2seventy under the licensed intellectual property will remain in effect in accordance with their respective terms. Additionally, all of 2seventy's payment obligations that have not yet accrued related to future milestone and royalty payments will be reduced by 50% for the remainder of the agreement term.

The Company concluded that 2seventy is a customer, and the contract is not subject to guidance on collaborative arrangements. This is because the Company granted 2seventy a license to the Company's intellectual property and provided research and development services, all of which are outputs of the Company's ongoing activities, in exchange for consideration.

The Company identified the following three material promises under the 2seventy Agreement: (i) transfer of a license to intellectual property and related technology know-how ("License and Know-How"); (ii) the obligation to perform target selection and TCR generation services ("Research and Development Services"); and (iii) participation on the Joint Steering Committee (the "JSC"). The Company provided to 2seventy standard indemnification and protection of licensed intellectual property, which is part of assurance that the license meets the contract's specifications and is not an obligation to provide goods or services.

The Company considered that the License and Know-How has standalone functionality, was considered to be functional intellectual property, and is capable of being distinct. However, the Company determined that the License and Know-How is not distinct from the Research and Development Services or participation on the JSC within the context of the 2seventy Agreement, because 2seventy is dependent on the Company to execute the Research and Development Services and participate on the JSC in order for 2seventy to benefit from the License and Know-How. As such, the License and Know-How is combined with the Research and Development Services and participation on the JSC into a single performance obligation, and the transaction price under this arrangement will be allocated to this single performance obligation.

The Company has also determined that all other goods or services that are contingent upon 2seventy reaching various milestones are not considered performance obligations at the inception of the arrangement.

The transaction price at the inception of the 2seventy Agreement consisted of the upfront payment of $20.0 million and the $10.0 million received from 2seventy for the purchase of the Company's Series C convertible preferred stock. The sale of the Series C convertible preferred stock was not considered to be a performance obligation, as it was a separate financing component of the transaction. Accordingly, $10.0 million of the transaction price was allocated to the issuance of 768,115 shares of Series C convertible preferred stock at fair value of $13.04 per share and recorded in stockholders' equity.

The variable consideration related to the remaining development, regulatory, and sales-based milestones payments has not been included in the initial transaction price and continues to be fully constrained as of December 31, 2021. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon initiation of clinical trials for early-stage targets and 2seventy's development efforts. Any variable consideration

related to sales-based milestones (including royalties) will be recognized when the related sales occur, as they were determined to relate predominantly to the License and Know-How granted to 2seventy. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

For revenue recognition purposes, the Company determined that the duration of the 2seventy Agreement began on the effective date in August 2018 and ends upon completion of the Research and Development Services, which is also when the participation on the JSC is no longer an obligation. The contract duration is defined as the period in which parties to the contract have present enforceable rights and obligations. The Company also analyzed the impact of 2seventy terminating the agreement prior to August 2023 and determined, considering both quantitative and qualitative factors, that there were substantive non-monetary penalties to 2seventy for doing so.

Revenue is recognized when, or as, the Company satisfies its performance obligation by transferring the promised services to 2seventy. Revenue is being recognized over time using a cost-based input method, based on internal labor cost effort to perform the research services, since the internal labor cost incurred over time is thought to best reflect the transfer of services to 2seventy. In applying a cost-based input method of revenue recognition, we use actual costs incurred relative to budgeted costs to fulfill the combined performance obligation. A cost-based input method of revenue recognition requires us to make estimates of costs to complete the performance obligation. The cumulative effect of any revisions to estimated costs to complete the performance obligation will be recorded in the period in which changes are identified and amounts can be reasonably estimated. A significant change in these assumptions and estimates could have a material impact on the timing and amount of revenue recognized in future periods.

For the years ended December 31, 2022, 2021, and 2020, the Company recognized $7.7 million, $3.0 million, and $2.8 million, respectively, in collaboration revenue under the 2seventy Agreement. The amount of collaboration revenue recognized during the year ended December 31, 2022 included cumulative catch-up adjustments increasing collaboration revenue by $6.4 million due to revisions to estimated costs to complete the remaining performance obligation. The adjustments resulted in a decrease in the Company's loss from operations of $6.4 million and a decrease in loss per share of $0.07 for the year ended December 31, 2022. Deferred revenue of $1.0 million was recorded on the consolidated balance sheet in current liabilities as of December 31, 2022 and $8.7 million was recorded on the consolidated balance sheets in both current and long-term liabilities as of December 31, 2021, respectively. Deferred revenue relates to the performance obligations identified under the 2seventy Agreement and will be recognized over the period the performance obligations are expected to be satisfied, which is currently estimated to be through August 2023.

Changes in the deferred revenue balance during the year ended December 31, 2022 are as follows (in thousands):

	Deferred Revenue
Balance at December 31, 2021	$ 8,725
Additions	—
Deductions	(7,678)
Balance at December 31, 2022	$ 1,047

There were no receivables or net contract assets recorded as of December 31, 2022 or 2021 associated with the 2seventy Agreement.

Gilead Sciences, Inc.

In January 2021, the Company entered into a Collaboration, Option and License Agreement (the "Gilead Collaboration Agreement") with Gilead Sciences, Inc. ("Gilead") to research and develop a vaccine-based immunotherapy as part of Gilead's efforts to find a curative treatment for HIV infection. Under the terms of the Gilead Collaboration Agreement, the Company granted to Gilead an exclusive, worldwide license to develop and commercialize a HIV-specific therapeutic vaccine utilizing the Company's technology. Gilead is responsible for conducting all development and commercialization activities beginning with a Phase 1 study, and the Company is responsible for contributing to preclinical research studies and participation in a joint steering committee (collectively, "research and development activities"). Concurrently with the execution of the Gilead Collaboration Agreement, the Company and Gilead entered into a Supply Agreement (the "Gilead Supply Agreement") under which the Company will supply research product and GMP product ("Product Supply") that may be required under the Gilead Collaboration Agreement until Gilead completes its first GMP product batch, and the Company will participate in a joint manufacturing team (collectively, "product supply activities"). In addition, the Company also concurrently entered into a Stock Purchase Agreement (the "Gilead Stock Purchase Agreement") under which Gilead acquired, in a private placement transaction, 1,169,591 shares of the Company's common stock. The common shares were issued to Gilead with

certain registration rights and certain standstill and market stand-off provisions. The Company determined that these concurrent contracts represent a combined arrangement (the "Gilead Arrangement").

Under the Gilead Collaboration Agreement, the Company received a non-refundable upfront payment of $30.0 million. Under the Gilead Collaboration Agreement and the Gilead Supply Agreement, the Company will receive additional reimbursement payments for expenses incurred in the research and development activities and product supply activities. Under the Gilead Stock Purchase Agreement, the common shares were sold at a price of $25.65 per share for a total of $30.0 million. The Company's common stock at fair value on closing was $18.10 per share. If Gilead decides to move forward with development beyond the initial Phase 1 study (the "Option"), the Company will receive a $40.0 million non-refundable option fee and will be eligible to receive up to an aggregate of $685.0 million if certain clinical, regulatory and commercial milestones are achieved, as well as tiered royalties ranging from the mid-single digits to low double-digits on net sales of a therapeutic product utilizing its technology. None of these events had occurred as of December 31, 2022 and no royalties were due from the sale of licensed products.

Gilead may terminate the Gilead Collaboration Agreement for convenience by giving a 90-day prior written notice to the Company at any time after the effective date of the agreement. Unless terminated early, the agreement has a term that ends upon the expiration of the royalty term, or, if the Option is not exercised, by the end of the Option term. The Gilead Collaboration Agreement may be terminated for cause by either party based on an uncured material breach by the other party, insolvency of the other party, or patent challenge. Upon early termination, all ongoing activities under the agreement and all mutual collaboration, development and commercialization licenses and sublicenses will terminate. The licenses granted by the Company to Gilead under the licensed intellectual property will remain in effect in accordance with their respective terms. Additionally, if terminated early by Gilead for convenience or by the Company for material breach or insolvency, all of Gilead's payment obligations for reimbursable costs or for future milestone and royalty payments remain. If terminated early by Gilead for material breach or insolvency, all of Gilead's unaccrued payment obligations related to future milestone and royalty payments will be reduced by 50% for the remainder of the agreement term. Furthermore, Gilead may terminate the Gilead Supply Agreement without cause by giving six months prior written notice and may terminate any active orders with 60-day notice without terminating the agreement, and either party may terminate based on an uncured material breach, insolvency of the other party, or in the event that the Gilead Collaboration Agreement is terminated. Upon termination, the Company will deliver all supply products that have been produced and destroy, reimburse or deliver materials that Gilead has reimbursed, and Gilead must pay for any manufacturing costs that the Company has actually incurred or committed to pay, including any cancellation costs owed to subcontractors.

The Company concluded that Gilead is a customer and therefore revenue recognition should be accounted for in accordance with ASC 606, because the Company granted to Gilead licenses to its intellectual property and will provide research and development services and Product Supply, all of which are outputs of the Company's ongoing activities, in exchange for consideration. The Option, if exercised by Gilead, will be considered a modification that increases the scope of the arrangement beyond the Option term.

The Company identified the following performance obligations under the Gilead Collaboration Agreement: (i) licenses including an exclusive (in the HIV field), royalty-free, worldwide collaboration license and transfer of know-how and an exclusive (in the HIV field) worldwide, royalty-bearing development and commercialization license subject to restrictions on its use during the Option term and an exclusive option to release such restrictions; (ii) preclinical research and development activities, manufacturing-related activities, and participation on a Joint Steering Committee; and (iii) product supply, including research and GMP product, until Gilead completes its first GMP batch, and participation on a Joint Manufacturing Team.

The Company considered that the licenses and know-how have standalone functionality, are considered to be functional intellectual property and are capable of being distinct. The Company also determined that the research and development activities and product supply by Gritstone could be provided by resources otherwise available to Gilead and thus are capable of being distinct.

The Company has also determined that the pricing for optional goods and services and release of license restrictions upon exercise of the Option do not constitute material rights and are not a potential performance obligation. The Company evaluated whether there is an interdependence between the promises and determined that the licenses are a combined solution and the predominant performance obligation, while the other promises are separately identifiable in the context of the contract; however, the research and development activities are dependent on the research product supply, which is accounted for as a combined performance obligation. As a result, the Company identified three performance obligations in the Gilead Arrangement: (i) exclusive licenses and know-how, (ii) research and development activities and product supply, and (iii) GMP product supply.

The transaction price at the inception of the Gilead Collaboration Agreement consisted of the upfront payment of $30.0 million and the $30.0 million received for the sale of the Company's common stock. The sale of the common stock was not considered to be a performance obligation, as it was a separate financing component of the transaction. Accordingly, $21.2 million of the transaction price was allocated to the issuance of 1,169,591 shares of the Company's common stock at fair value on closing of $18.10 per share and recorded in stockholders' equity. The remaining $8.8 million of the common stock purchase price in excess of the fair value of the shares received is added to the transaction price for the Gilead Collaboration Agreement. In addition, the initial transaction price includes estimated variable consideration for budgeted reimbursement of research and development costs and product supply. The variable consideration related to reimbursable costs and product supply has been constrained as of December 31, 2022 based on the current research and development plan forecast. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

The Company determined that the variable consideration for the $40.0 million option exercise fee and for the development, regulatory, and sales-based milestones payments were probable of significant revenue reversal as their achievement was highly dependent on factors outside the Company's control. As a result, these payments were fully constrained and were not included in the transaction price. Any variable consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur, as they were determined to relate predominantly to the exclusive licenses and know-how granted to Gilead.

The transaction price is allocated to the performance obligation based upon relative standalone selling prices, which were determined for the exclusive licenses and know-how using an adjusted market approach and for the research and development activities and product supply using a cost plus reasonable margin approach. Variable consideration is allocated to the specific performance obligations to which it relates.

For revenue recognition purposes, the Company determined that the duration of the contract began on the effective date in January 2021 and ends upon (i) the completion of the Option term, which is expected to end two to four years after the effective date, if the Option is not exercised or (ii) the expiration of the royalty-term on a product-by-product and country-by-country basis. The Company also analyzed the impact of Gilead terminating the agreement prior to the end of the Option term and determined, considering both quantitative and qualitative factors, that there were substantive non-monetary penalties to Gilead for doing so.

Revenue for the exclusive licenses and know-how was recognized on the effective date of the Gilead Collaboration Agreement at the point in time that the licenses are effective. The research and development activities and product combined performance obligation and the GMP product supply performance obligation are recognized over time when, or as, the Company transfers the promised goods and services to Gilead. Research and development service and product supply revenues will be recognized over time using a cost-based input method, based on internal and external labor cost effort to perform the services, costs to acquire research materials, and costs of product supply, since the costs incurred over time are thought to best reflect the transfer of goods and services to Gilead. In applying a cost-based input method of revenue recognition, we use actual costs incurred relative to estimated total costs to fulfill each performance obligation. A cost-based input method of revenue recognition requires us to make estimates of costs to complete the performance obligation. The cumulative effect of any revisions to estimated costs to complete the performance obligation and associated variable consideration will be recorded in the period in which changes are identified and amounts can be reasonably estimated. A significant change in these assumptions and estimates could have a material impact on the timing and amount of revenue recognized in future periods.

For the year ended December 31, 2022, the Company did not record any license revenue. For the year ended December 31, 2022, the Company recorded $1.6 million as collaboration revenue as a result of satisfying its performance obligations by transferring the promised goods and services estimated by the costs incurred for the Gilead Collaboration Agreement. For the year ended December 31, 2021, the Company recognized $38.6 million as license revenue, and $5.1 million as collaboration revenue as a result of satisfying its performance obligations by transferring the promised goods and services estimated by the costs incurred for the Gilead Collaboration Agreement. There was no contract asset recorded on the consolidated balance sheet as of December 31, 2022. A contract asset of $1.4 million was recorded on the consolidated balance sheet as a current asset in the prepaid expenses and other current assets balance as of December 31, 2021 for supply costs that were incurred during the year ended December 31, 2021, but not billable until future periods when the asset is released. The contract asset relates to the performance obligations yet to be satisfied under the Gilead Collaboration Agreement. There was $0.1 million recorded as deferred revenue as of December 31, 2022 and no deferred revenue as of December 31, 2021 associated with the Gilead Collaboration Agreement.

Changes in the contract asset and short-term deferred revenue, balance during the year ended December 31, 2022 for the Gilead Collaboration Agreement are as follows (in thousands):

	Contract Asset	Deferred Revenue
Balance at December 31, 2021	$ 1,385	$ —
Additions	123	122
Deductions	(1,508)	(15)
Balance at December 31, 2022	$ —	$ 107

There was $0.1 million and $0.7 million of receivables recorded on the consolidated balance sheet as a current asset in the prepaid expenses and other current assets balance as of December 31, 2022 and 2021, respectively.

The Company deferred $0.1 million in incremental costs to acquire the Gilead Collaboration Agreement in the first quarter of 2021 allocated to performance obligations recognized over time, which will be recognized over time in each period proportionate to revenue recognition. As of December 31, 2022, deferred contract acquisition costs were zero. Deferred contract acquisition costs amortized during the year ended December 31, 2022 and 2021 were negligible.

Arbutus Biopharma Corporation

In October 2017, the Company entered into an Exclusive License Agreement with Arbutus and its wholly-owned subsidiary, Protiva Biotherapeutics Inc. Certain terms of the agreement were modified by amendment in July 2018. Under the license agreement, the Company has an exclusive license to utilize certain Arbutus intellectual property, including patents and know-how relating to immunotherapy. During the years ended December 31, 2022, 2021 and 2020, the Company had no research and development expense under the agreement. The Company is obligated to pay Arbutus certain milestone payments up to $123.5 million on achievement of specified events, and royalties on sales of its licensed products. Following the acceptance of our investigational new drug application for GRANITE by the FDA, the Company made a $2.5 million development milestone payment to Arbutus in September 2018 that was recorded as research and development expense. In August 2019, a milestone was met following the initial patient treatment of SLATE in the Company's GO-005 clinical trial. In 2019, the Company recorded $3.0 million as research and development expense in connection with the milestone. None of the other events had occurred as of December 31, 2022, and no royalties were due from the sale of licensed products.

Non-Profit Hospital Cancer Center

In January 2016, the Company entered into an Exclusive License Agreement with a non-profit hospital cancer center. Under the license agreement, the Company has an exclusive license to utilize certain patents and know-how relating to immunotherapy for an insignificant upfront payment, cash milestone payments on achievement of specified events, and a low single digit royalty on sales of licensed products. The achievement of the milestones and payment of royalties is dependent upon obtaining regulatory approval. Upon achievement of a milestone related to the Company's Phase 1 clinical trial for GRANITE, GO-004, in December 2018 the Company recorded an insignificant amount to research and development expense for amounts owed to the Hospital Cancer Center, which was paid to the hospital in February 2019. None of the other milestone events had occurred as of December 31, 2022, and no royalties were due from the sales of licensed products.

Genevant Sciences GmbH

In October 2020, the Company entered into an Option and License and Development Agreement (the "2020 Genevant License Agreement") with Genevant Sciences GmbH ("Genevant"), pursuant to which Genevant granted the Company exclusive license rights under certain intellectual property related to Genevant's LNP technology for a single therapeutic indication, and the Company agreed to pay Genevant an initial payment of $2.0 million, up to an aggregate of $71.0 million in specified development, regulatory, and commercial milestones, and low to mid-single digit royalties on net sales of licensed products. The upfront payment of $2.0 million was included in research and development expense for the year ended December 31, 2020. Genevant is a spin-off of Arbutus, and the 2020 Genevant License Agreement expands Gritstone's intellectual property rights to such LNP technology originally obtained pursuant to the Company's license agreement with Arbutus. Prior to the 2020 Genevant License Agreement, the Company licensed Arbutus' LNP technology for indications in the oncology space. The remainder of Arbutus' IP portfolio was transferred to Genevant in the spin-off. In

March 2022, a milestone in the amount of $1.0 million was met, which was included in research and development expense for the year ended December 31, 2022.

Pursuant to the 2020 Genevant License Agreement, Genevant also granted the Company certain options to license the LNP technology for additional therapeutic indications of up to $1.5 million for each indication and $1.0 million to extend the option term. The 2020 Genevant License Agreement continues in effect until the last to expire royalty term or early termination. It is terminable by the Company for convenience with 90 days prior written notice or immediately if based on certain product safety or efficacy or regulatory criteria. Either party may terminate the agreement for material breach, subject to a cure period, and Genevant may terminate the agreement if the Company challenges a licensed patent.

In January 2021, the Company entered into a Non-Exclusive License and Development Agreement (the "2021 Genevant License Agreement") with Genevant. Pursuant to the 2021 Genevant License Agreement, the Company obtained a nonexclusive license to Genevant's LNP technology to develop and commercialize self-amplifying RNA ("samRNA") vaccines against SARS-CoV-2, the virus that causes COVID-19. Under the 2021 Genevant License Agreement, the Company made a $1.5 million upfront payment to Genevant, and Genevant is eligible to receive from the Company up to an aggregate of $141.0 million in contingent milestone payments per product, plus certain tiered royalties, upon achievement of development and commercial milestones. In certain scenarios, in lieu of milestones and royalties, Genevant will be entitled to a percentage of amounts that the Company receives from sublicenses under the 2021 Genevant License Agreement, subject to certain conditions. In March 2021, a milestone in the amount of $1.0 million was met following the initial patient treatment in the Phase 1 clinical trial conducted through the NIAID-supported Infectious Diseases Clinical Research Consortium ("IDCRC"). Both the $1.5 million upfront and $1.0 million milestone payments were recorded as research and development expense for the year ended December 31, 2021. None of the other milestone events had occurred as of December 31, 2022.

Coalition for Epidemic Preparedness Innovations

On August 14, 2021, the Company entered into the CEPI Funding Agreement with CEPI, under which CEPI agreed to provide funding of up to $20.6 million to the Company to advance the Company's CORAL program, a second-generation COVID-19 vaccine program, with an initial clinical trial in South Africa. Under the terms of the agreement, CEPI is funding a multi-arm Phase 1 study evaluating the CORAL program's samRNA vaccine in naïve, convalescent, and HIV+ patients. The study is evaluating three different samRNA vaccine constructs that each target both the spike protein and other SARS-CoV-2 targets and are designed to drive both robust B and T cell immune responses. The funding is also supporting pre-clinical studies, scale-up and formulation development to enable manufacturing of large quantities of stable vaccine product.

Under the terms of the CEPI Funding Agreement, among other things, the Company and CEPI agreed on the importance of global equitable access to the vaccine produced pursuant to the CEPI Funding Agreement. The vaccine, if approved, is expected to be made available to the COVAX Facility for procurement and allocation. The COVAX Facility aims to deliver equitable access to COVID-19 vaccines for all countries, at all levels of development, that wish to participate.

The scope and continuation of the CEPI Funding Agreement may be amended depending on ongoing developments of the COVID-19 outbreak and the success of the Company's COVID-19 vaccine candidate developed under the CEPI Funding Agreement relative to other third-party COVID-19 vaccine candidates or treatments. If the World Health Organization ("WHO"), CEPI or a regulatory authority having jurisdiction over a clinical trial performed under the CEPI Funding Agreement determines that a third-party product candidate has substantially greater potential than the Company's COVID-19 vaccine candidate developed under the CEPI Funding Agreement and should be prioritized instead for a particular trial, the Company must consider in good faith any written request of CEPI not to proceed with a clinical trial of such COVID-19 vaccine candidate; however the determination of whether or not to proceed with such trial shall be made by the Company in its sole discretion. In addition, CEPI has the right to unilaterally terminate the CEPI Funding Agreement upon prior written notice if CEPI determines that (i) there are material safety, regulatory, scientific misconduct or ethical issues with the project undertaken by the Company under the CEPI Funding Agreement, (ii) the project undertaken by the Company under the CEPI Funding Agreement should be terminated, (iii) the Company becomes unable to discharge its obligations under the CEPI Funding Agreement, (iv) the Company fails to meet certain criteria set forth in the CEPI Funding Agreement, or (v) the Company commits fraud or a financial irregularity, as such terms are defined in the CEPI Funding Agreement.

In December 2021, the Company and CEPI entered into an amendment to the CEPI Funding Agreement, under which CEPI agreed to provide additional funding up to $5.0 million, for a total of up to $25.6 million, to the Company to conduct a Phase I clinical trial of the Company's Omicron vaccine candidate in South Africa.

CEPI advances grant funds upon request by the Company consistent with the agreed upon amounts and schedules as provided in the CEPI Funding Agreement. The first tranche of funding of $11.3 million was received in September 2021, and the second tranche of funding of $2.7 million was received in April 2022.

Payments received in advance that are related to future performance are deferred and recognized as grant revenue when the research and development activities are performed. Cash payments received under the CEPI Funding Agreement are restricted as to their use until expenditures contemplated in the agreement are incurred. During the year ended December 31, 2022, the Company recognized grant revenue of $9.5 million under the CEPI Funding Agreement. During the year ended December 31, 2021, the Company recognized $1.5 million in grant revenue under the CEPI Funding Agreement. As of December 31, 2022 and 2021, short term deferred revenue of $3.0 million and $9.4 million, respectively, recorded on the consolidated balance sheets. Deferred revenue will be recognized over the period in which the CEPI Funding Agreement activities related to the first and second tranches of funding are expected to take place, which is currently estimated to be through the year ended 2023. As of December 31, 2022 and 2021, $3.0 million and $9.4 million, respectively, was recorded as short-term restricted cash on the consolidated balance sheet.

Changes in the short-term deferred revenue, balance during the year ended December 31, 2022 for the CEPI Funding Agreement are as follows (in thousands):

	Deferred Revenue
Balance at December 31, 2021	$ 9,379
Additions	2,698
Deductions	(9,125)
Balance at December 31, 2022	$ 2,952

Gates

In November 2021, the Company entered into a Grant Agreement with the Gates Foundation (the “Gates Grant Agreement”), which provides funding for the Company’s development of an optimal immunogen in the context of a therapeutic human papillomavirus (“HPV”) vaccine. In consideration for the work to be performed, the Gates Foundation provided the Company with an upfront payment of $2.2 million in December 2021, and future funding of $1.0 million is expected to be received by the Company in the first quarter of 2023, for a total grant amount of up to $3.2 million.

Payments received in advance that are related to future performance are deferred and recognized as grant revenue when the research and development activities are performed. Cash payments received under the Gates Grant Agreement are restricted as to their use until expenditures contemplated in the funding agreement are incurred. During the year ended December 31, 2022, the Company recognized $1.2 million in revenue under the Gates Grant Agreement. The Company did not recognize any grant revenue under the Gates Grant Agreement in 2021. As of December 31, 2022, short-term restricted cash and short-term deferred revenue of $1.0 million were recorded on the consolidated balance sheet. As of December 31, 2021, short-term restricted cash and short-term deferred revenue of $1.9 million and long-term restricted cash and long-term deferred revenue of $0.3 million were recorded on the consolidated balance sheet. Deferred revenue will be recognized over the period in which the funding agreement activities related to the tranches of funding are expected to take place, which is currently estimated to be through the year ended 2023.

Changes in the short-term deferred revenue, balance during the year ended December 31, 2022 for the Grant Agreement are as follows (in thousands):

	Deferred Revenue
Balance at December 31, 2021	$ 2,225
Additions	—
Deductions	(1,200)
Balance at December 31, 2022	$ 1,025

8. Debt

In July 2022, the Company entered into a loan and security agreement (the “Loan Agreement”) with Hercules Capital, Inc. (“Hercules”) and Silicon Valley Bank (“SVB”), which provides the Company a 60-month term loan facility for up to $80.0 million in

borrowing capacity across five potential tranches. At the closing of the Loan Agreement, the Company drew $20.0 million from the first tranche and can draw up to an additional $10.0 million through March 2023. The remaining tranches provide up to $50.0 million borrowing capacity and become available upon the Company meeting certain milestones set forth in the Loan Agreement. As of December 31, 2022, one milestone had been achieved, which provides the Company the ability to draw up to $10 million through December 15, 2023. The term loan is secured by substantially all of the Company's assets, other than intellectual property. There are no warrants associated with the Loan Agreement.

Borrowings under the Loan Agreement bear interest (i) at an annual cash rate equal to the greater of (x) the lesser of (1) the prime rate (as customarily defined) and (2) 5.50%, in either case, plus 3.15%, and (y) 7.15% and (ii) at an annual payment-in-kind rate which may equal 2.00%. The Company is required to make monthly interest-only payments prior to the amortization date of January 1, 2025, subject to a potential six-month and one-year extension upon satisfaction of certain conditions. The interest-only payment date has been extended an additional six months based on our achievement of one of the milestones as set forth in the Loan Agreement. In addition, the Company paid a $150,000 facility charge upon closing, and must pay a facility charge equal to 0.50% of the principal amount of any borrowings made pursuant to the amounts under the last four tranches.

All unpaid principal and accrued and unpaid interest with respect to each term loan is due and payable in full on July 19, 2027. At the Company's option, the Company may prepay all or any portion of the outstanding borrowings, plus accrued and unpaid interest thereon and fees and expenses, subject to a prepayment premium ranging from zero to 2.5%, during the first three years after closing, depending on the year of such prepayment. Upon repayment of the term loan, the Company is required to make a final payment fee to the lenders equal to 5.75% of the aggregate original principal amount of the loan. Debt issuance costs have been treated as debt discounts on the Company's consolidated balance sheet and together with the final payment are being amortized to interest expense throughout the life of the term loan using the effective interest rate method.

Beginning on April 1, 2023, so long as the Company's market capitalization is equal to or less than $400.0 million, the Company is subject to a minimum liquidity requirement equal to the then outstanding balance under the Loan Agreement multiplied by 0.55 or 0.45, which multiplier depends on whether the Company achieves certain performance milestones.

The Company's obligations under the Loan Agreement are subject to acceleration upon the occurrence of customary events of default, including payment default, insolvency and the occurrence of certain events having a material adverse effect on the Company, including (but not limited to) material adverse effects upon the business, operations, properties, assets or financial condition of the Company and its subsidiaries, taken as a whole. As of December 31, 2022, the Company is in compliance with all covenants in the Loan Agreement.

As of December 31, 2022, there were unamortized issuance costs and debt discounts of $1.8 million which were recorded as a direct deduction from the term loan on the consolidated balance sheet. Interest expense related to the Loan Agreement was $1.2 million for the year ended December 31, 2022. The effective interest rate on the term loan, including the amortization of the debt discount and issuance costs, and accretion of the final payment, was 13%. The components of the long-term debt balance are as follows:

	December 31, 2022
Principal loan balance	$ 20,000
Final fee	1,150
Unamortized debt discount and issuance costs	(1,801)
Long term debt, net	$ 19,349

As of December 31, 2022, the estimated future principal payments due (excluding the final payment fee) were as follows:

2023	$ —
2024	—
2025	4,407
2026	9,396
2027	6,197
Total principal payments	$ 20,000

9. Balance Sheet Components

Prepaid Expenses and Other Assets

Prepaid expenses and other current assets consist of the following (in thousands):

	December 31,	
	2022	2021
Prepaid research and development-related expenses	$ 4,241	$ 2,672
Net contract asset	—	1,385
Collaboration receivable	135	688
Prepaid insurance	1,158	1,769
Interest and other receivables	529	292
Facilities-related deposits	384	—
Other	567	866
Total prepaid expenses and other current assets	$ 7,014	$ 7,672

Deposits and Other Long-Term Assets

Deposits and other long-term assets consist of the following (in thousands):

	December 31,	
	2022	2021
Lease security deposits	$ 934	$ 1,305
Prepaid research and development-related expenses	643	1,047
Prepaid rent	8,162	—
Total deposits and other long-term assets	$ 9,739	$ 2,352

10. Stockholders' Equity

The Company's amended and restated certificate of incorporation provides for 300,000,000 shares of common stock and 10,000,000 shares of preferred stock authorized for issuance, each with a par value of $0.0001 per share.

As of December 31, 2022 and 2021, no shares of preferred stock were issued and outstanding.

As of December 31, 2022 and 2021, there were 86,894,901 and 69,047,878 shares of common stock issued and outstanding, respectively. Holders of the Company's common stock are entitled to one vote per share.

Sale of Common Stock and Pre-Funded Warrants

In October 2019, the Company filed a Registration Statement on Form S-3 (the "2019 Shelf Registration Statement") with the SEC, covering the offering of up to $250.0 million of common stock, preferred stock, debt securities, warrants and units. The 2019 Shelf Registration Statement included a prospectus covering the offering, issuance and sale of up to $75.0 million of the Company's common stock, from time to time, through the ATM Offering Program under the Securities Act of 1933, as amended (the "Securities Act"). The SEC declared the 2019 Shelf Registration Statement effective on November 8, 2019.

In connection with the 2019 ATM Offering Program, in October 2019, the Company entered into a sales agreement (the "2019 Sales Agreement") with Cowen and Company, LLC ("Cowen"), pursuant to which Cowen acts as the Company's sales agent and, from time to time, offers and sells shares of the Company's common stock having an aggregate offering price of up to $75.0 million. Cowen is entitled to compensation for its services equal to up to 3.0% of the gross proceeds of any shares of common stock sold under the 2019 Sales Agreement. In addition, the Company agreed to reimburse a portion of Cowen's expenses in connection with the 2019 ATM Offering Program up to $50,000. During the year ended December 31, 2021, the Company issued and sold 3,990,869 shares of its common stock through its 2019 ATM Offering Program and received net proceeds of approximately $36.6 million, net of commissions and other offering costs. During the year ended December 31, 2022, there have been no sales of shares of the Company's common stock

through its 2019 ATM Offering Program. As of December 31, 2022, there are no further amounts available for issuance under the 2019 ATM Offering Program.

In December 2020, the Company entered into two private placement financing transactions (collectively, the "First PIPE Financing"), as follows: (i) to sell 5,543,351 shares of its common stock at a price of $3.34 per share and pre-funded warrants (the "Warrants") to purchase 27,480,719 shares of common stock at a price of $3.34 per share (of which $3.33 per share was prepaid by each purchaser), and (ii) to sell an additional 4,043,127 shares of its common stock at a price per share of $3.71. In connection with the First PIPE Financing, the Company received aggregate net proceeds of approximately $119.8 million. The Warrants are exercisable upon issuance at an exercise price of $0.01 per share.

The outstanding Warrants generally may not be exercised if the holder's aggregate beneficial ownership would be more than 9.99% of the total issued and outstanding shares of the Company's common stock following such exercise. The exercise price and number of shares of common stock issuable upon the exercise of the Warrants (the "Warrant Shares") are subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Warrant agreements. Under certain circumstances, the Warrants may be exercisable on a "cashless" basis. In connection with the issuance and sale of the common stock and Warrants, the Company granted the purchasers certain registration rights with respect to the Warrants and the Warrant Shares.

The Warrants were classified as a component of permanent stockholders' equity within additional paid-in-capital and were recorded at the issuance date using a relative fair value allocation method. The Warrants are equity classified because they are freestanding financial instruments that are legally detachable and separately exercisable from the equity instruments, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, permit the holders to receive a fixed number of common shares upon exercise, are indexed to the Company's common stock and meet the equity classification criteria. In addition, such Warrants do not provide any guarantee of value or return. The Company valued the Warrants at issuance, concluding their sales price approximated their fair value, and allocated net proceeds from the sale proportionately to the common stock and Warrants, of which $87.7 million, net of issuance costs, was allocated to the Warrants and recorded as a component of additional paid-in-capital.

In September 2021, the Company completed a PIPE financing transaction, in which it sold 5,000,000 shares of its common stock at a price of $11.00 per share pursuant to a securities purchase agreement entered into on September 16, 2021 (the "Second PIPE Financing"). The Company received aggregate net proceeds of approximately $52.7 million after deducting placement agent commissions and offering expenses payable by the Company. In connection with the issuance and sale of the common stock, the Company agreed to file a registration statement with the SEC registering the resale of the shares of common stock issued in the Second PIPE Financing.

In March 2022, the Company filed a Registration Statement on Form S-3 with the SEC (the "2022 Shelf Registration Statement"), covering the offering of up to $250.0 million of common stock, preferred stock, debt securities, warrants and units. The 2022 Shelf Registration Statement included a prospectus supplement covering the issuance and sale of up to $100.0 million of the Company's common stock, from time to time, through an "at-the-market" offering program (the "2022 ATM Offering Program") under the Securities Act. The SEC declared the 2022 Shelf Registration Statement effective as of May 6, 2022.

In connection with the 2022 ATM Offering Program, in March 2022, the Company also entered into a sales agreement (the "2022 Sales Agreement") with Cowen, pursuant to which Cowen will act as the Company's sales agent and, from time to time, offer and sell shares of the Company's common stock having an aggregate offering price of up to $100.0 million. Cowen is entitled to compensation for its services equal to up to 3.0% of the gross proceeds of any shares of common stock sold under the 2022 Sales Agreement. In addition, the Company agreed to reimburse a portion of Cowen's expenses in connection with the 2022 ATM Offering Program up to $50,000. As of December 31, 2022, the Company has received aggregate proceeds from its 2022 ATM Offering Program of $19.6 million, net of commissions and offering costs, pursuant to the issuance of 7,034,948 shares of its common stock.

In October 2022, the Company completed a PIPE financing transaction, in which it sold 6,637,165 shares of its common stock at a price of $2.26 per share pursuant to a securities purchase agreement entered into on October 24, 2022 and pre-funded warrants (the "Warrants") to purchase 13,274,923 shares of common stock at a price of $2.26 per share (of which $2.2599 per share was prepaid by each purchaser) (the "Third PIPE Financing"). The Company received aggregate net proceeds of approximately $42.4 million after deducting placement agent commissions and offering expenses payable by the Company. In connection with the issuance and sale of the common stock, the Company agreed to file a registration statement with the SEC registering the resale of the shares of common stock issued in the Third PIPE Financing. The Warrants are exercisable upon issuance at an exercise price of $0.0001 per share.

The outstanding Warrants generally may not be exercised if the holder's aggregate beneficial ownership would be more than 9.99% of the total issued and outstanding shares of the Company's common stock following such exercise. The exercise price and number of shares of common stock issuable upon the exercise of the Warrants (the "Warrant Shares") are subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Warrant agreements. Under certain circumstances, the Warrants may be exercisable on a "cashless" basis. In connection with the issuance and sale of the common stock and Warrants, the Company granted the purchasers certain registration rights with respect to the Warrants and the Warrant Shares.

The Warrants were classified as a component of permanent stockholders' equity within additional paid-in-capital and were recorded at the issuance date using a relative fair value allocation method. The Warrants are equity classified because they are freestanding financial instruments that are legally detachable and separately exercisable from the equity instruments, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, permit the holders to receive a fixed number of common shares upon exercise, are indexed to the Company's common stock and meet the equity classification criteria. In addition, such Warrants do not provide any guarantee of value or return. The Company valued the Warrants at issuance, concluding their sales price approximated their fair value, and allocated net proceeds from the sale proportionately to the common stock and Warrants, of which $28.2 million, net of issuance costs, was allocated to the Warrants and recorded as a component of additional paid-in-capital.

Common Stock Warrants

As of December 31, 2022, the following warrants to purchase shares of the Company's common stock were issued and outstanding:

Issue Date	Expiration Date	Exercise Price	Number of Warrants Outstanding
December 28, 2020	None	$ 0.01	13,573,704
October 24, 2022	None	$ 0.0001	13,274,923
			26,848,627

During the year ended December 31, 2022, there were 3,442,567 warrants exercised, resulting in the Company issuing 3,442,567 shares of common stock. During the year ended December 31, 2021, there were 10,459,576 warrants exercised and 4,872 warrants cancelled due to net exercise of the warrants.

11. Stock-Based Compensation

Award Incentive Plans

In August 2015, the Company's board of directors approved the 2015 Equity Incentive Plan ("2015 Plan"). In connection with the Company's IPO and the effectiveness of the 2018 Award Incentive Plan ("2018 Plan"), discussed below, the 2015 Plan terminated. The 92,815 shares of common stock that were then unissued and available for future issuance under the 2015 Plan became available under the 2018 Plan.

In September 2018, the Company's board of directors approved the 2018 Plan. Under the 2018 Plan, a total of 2,690,000 shares of common stock were initially reserved for issuance under the 2018 Plan, plus the number of shares remaining available for future awards under the 2015 Plan, as of the effective date of the 2018 Plan. The number of shares of common stock reserved for issuance under the 2018 Plan automatically increases on January 1 of each year, beginning on January 1, 2019 and continuing through and including January 1, 2028, by 4% of the total number of shares of the Company's outstanding stock on December 31 of the preceding calendar year, or a lesser number of shares determined by the Company's board of directors. The 2018 Plan provides, among other things, for the grant of options, stock appreciation rights, restricted stock awards, restricted stock unit awards and performance bonus awards.

The maximum number of shares that may be issued upon the exercise of stock options under the 2018 Plan is 45,000,000.

The Company's board of directors has the authority to determine to whom options will be granted, the number of shares, the term, and the exercise price. If an individual owns stock representing 10% or more of the outstanding shares, the price of each share

shall be at least 110% of the fair market value, as determined by the board of directors. Options granted have a term of up to 10 years and generally vest over a 4-year period with a straight-line vesting.

Material Features of the 2021 Employment Inducement Incentive Award Plan

In April 2021, the Company's board of directors adopted the 2021 Employment Inducement Incentive Award Plan (the "2021 Plan"), pursuant to Nasdaq Listing Rule 5635(c)(4). The principal purpose of the 2021 Plan is to promote the success and enhance the value of the Company by inducing new employees to commence employment with us, and by aligning the individual interests of new employees with the interests of our stockholders. Awards granted under the 2021 Plan are intended to constitute "employment inducement awards" under Nasdaq Listing Rule 5635(c)(4), and, therefore, the 2021 Plan is intended to be exempt from the Nasdaq Listing Rules regarding shareholder approval of stock option and stock purchase plans. A total of 790,400 shares of our common stock were initially reserved for issuance under the 2021 Plan. The 2021 Plan provides for the grant of non-qualified stock options, restricted stock units, restricted stock awards, stock appreciation rights, and other stock-based and cash-based awards. The 2021 Plan does not provide for the grant of incentive stock options. Awards under the 2021 Plan may be granted to eligible employees who are either new employees or who are commencing employment with us or one of our subsidiaries following a bona fide period of non-employment with us, and for whom such awards are granted as a material inducement to commencing employment with us or one of our subsidiaries. Awards under the 2021 Plan may not be granted to our consultants or non-employee directors.

The 2021 Plan is administered by our board of directors and, to the extent our board of directors delegates its authority to it, our compensation committee. In the event of a change in control in which the successor corporation refuses to assume or substitute any outstanding award under the 2021 Plan, the vesting of such award will accelerate in full. Our board of directors may terminate, amend, or modify the 2021 Plan at any time, provided that no termination or amendment may materially impair any rights under any outstanding award under the 2021 Plan without the consent of the holder.

On April 21, 2022, the Company's board of directors increased the number of shares available under the 2021 Plan by 700,000 shares.

2018 Employee Stock Purchase Plan

In September 2018, the Company's Board of Directors approved the 2018 Employee Stock Purchase Plan ("2018 ESPP"). The 2018 ESPP also became effective in September 2018. A total of 282,334 shares were initially reserved for issuance under the 2018 ESPP. Additionally, the number of shares of common stock reserved for issuance under the 2018 ESPP will increase automatically each year, beginning on January 1, 2019 and continuing through and including January 1, 2028, by the lesser of (1) 1% of the shares of common stock outstanding on December 31 of the preceding calendar year or (2) such lesser number of shares determined by the Company's Board of Directors. The maximum number of shares that may be issued under the 2018 ESPP is 5,000,000. The offering periods are scheduled to start on the first trading day on or after June 1 or December 1 of each year. Contributions under the 2018 ESPP are limited to a maximum of 15% of an employee's eligible compensation.

The estimated fair value of stock purchase rights granted under the 2018 ESPP were calculated using the Black-Scholes option-pricing model using the following assumptions:

	Year ended December 31,		
	2022	2021	2020
Expected dividend yield	—%	—%	—%
Expected term	0.50 years	0.57 years	0.48 years
Risk-free interest rate	1.3%	0.1%	0.8%
Expected volatility	94.9%	88.0%	81.0%

Valuation of Stock Options

The fair value of each stock option granted to an employee or a director was estimated as of the date of grant using the Black-Scholes model with the following weighted-average assumptions:

	Year Ended December 31,		
	2022	2021	2020
Expected dividend yield	—%	—%	—%
Expected term	5.98 years	6.01 years	6.01 years
Risk-free interest rate	2.1%	1.1%	1.1%
Expected volatility	77.9%	79.0%	73.0%

Management's calculations are based on a grant date valuation approach. Using the Black-Scholes model, the weighted-average grant-date fair value of employee stock options granted was $3.20, $8.03, and $5.39 per share during the years ended December 31, 2022, 2021, and 2020, respectively.

Stock Option Activity

A summary of the 2018 Plan and 2021 Plan activity is as follows:

		Options Outstanding			
	Number of Shares Available for Issuance	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2021	3,459,187	5,107,335	$ 9.82	8.13	$ 17,153
Authorized	3,461,915	—	$ —		
Granted	(3,518,734)	3,168,561	$ 4.73		
Exercised		(194,347)	$ 0.96		
Cancelled	1,412,026	(1,129,929)	$ 8.73		
Balance at December 31, 2022	4,814,394	6,951,620	$ 7.92	8.08	$ 1,089
Vested and exercisable – December 31, 2022		3,122,952	$ 9.24	7.16	$ 409
Vested and expected to vest – December 31, 2022		6,421,425	$ 8.04	8.00	$ 995

For the years ended December 31, 2022, 2021, and 2020, the total intrinsic value of stock option awards exercised was $0.5 million, $5.8 million, and $0.9 million, respectively, determined at the date of option exercise, and the total cash received upon exercise of stock options was $0.2 million in 2022, $3.4 million in 2021 and not significant for 2020. The aggregate intrinsic value was calculated as the difference between the exercise prices of the underlying stock option awards and the estimated fair value of the common stock on the date of exercise.

As of December 31, 2022, $14.5 million of total cost related to non-vested employee and consultant options is expected to be recognized over a weighted-average period of 2.4 years. The total fair value of shares vested during the year ended December 31, 2022 was $9.9 million.

Stock-based compensation expense and awards granted to non-employees was $0.6 million for the year ended December 31, 2022, $0.7 million for the year ended December 31, 2021, and immaterial for the year ended December 31, 2020.

Restricted Stock Units

We have granted restricted stock unit awards under the 2018 Equity Plan. Our restricted stock unit awards have a term of up to 10 years and generally vest over a 1 or 2-year period. The following table summarizes our restricted stock unit activity during the year ended December 31, 2022:

	Number of Shares	Weighted Average Grant Date Fair Value
Outstanding, unvested as December 31, 2021	708,800	$ 5.29
Issued	350,173	$ 5.46
Vested	(353,300)	$ 5.29
Canceled/Forfeited	(144,147)	$ 5.35
Outstanding, unvested as December 31, 2022	561,526	$ 5.38

Stock-Based Compensation Expense

Total stock-based compensation for all awards granted to employees, consultants and our 2018 ESPP, before taxes, is as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Research and development expenses	$ 6,730	$ 6,626	$ 4,453
General and administrative expenses	5,827	3,926	2,657
Total	$ 12,557	$ 10,552	$ 7,110

12. Income Taxes

The effective tax rate for the years ended December 31, 2022, 2021, and 2020 is different from the federal statutory rate primarily due to the valuation allowance against deferred tax assets as a result of insufficient sources of income. The effective tax rate of the Company's provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,		
	2022	2021	2020
Statutory federal income tax rate	21.0%	21.0%	21.0%
State tax, net of federal benefit	7.6	10.2	7.9
Permanent differences	(0.4)	(0.1)	(0.6)
Research and development tax credits	1.2	1.9	2.8
Other	(1.1)	(1.8)	(0.2)
Change in state tax apportionment	—	—	9.4
Non-taxable stock premium	—	2.5	—
Change in valuation allowance	(28.3)	(33.7)	(40.3)
Total provision for income taxes	—%	—%	—%

The Company uses the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company assesses the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

In assessing the realizability of deferred tax assets, the Company considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible. Due to the Company's history of losses, and lack of other positive evidence, the Company has determined that it is more likely than not that its net deferred tax assets will not be realized, and therefore, the net deferred tax assets are fully offset by a valuation allowance at December 31, 2022 and 2021. The deferred tax assets were primarily comprised of federal and state tax net operating losses

and tax credit carryforwards. The increase in valuation allowance of $33.9 million and $25.2 million during 2022 and 2021, respectively, was primarily attributable to the Company's current year taxable loss and increase in the effective state tax rate due to changes in the Company's state apportionment factors.

The components of the net deferred tax assets/liabilities are as follows (in thousands):

	December 31,	
	2022	2021
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 109,191	$ 97,575
Research and development tax credits	14,877	12,271
Lease liabilities	6,031	7,684
Accruals and other	3,786	3,184
Amortization	9,437	10,633
Deferred revenue	700	2,537
Other depreciation	449	—
Section 174 Capitalized Expense	21,434	—
Gross deferred tax assets	165,905	133,884
Valuation allowance	(160,877)	(127,007)
Net deferred tax assets	5,028	6,877
Deferred tax liabilities:		
Other depreciation	—	(212)
Operating lease right-of-use assets	(5,028)	(6,665)
Deferred tax assets, net of allowance	$ —	$ —

Beginning January 1, 2022, the Tax Cuts and Jobs Act (the "Tax Act") eliminated the option to deduct research and development expenditures in the current year and requires taxpayers to capitalize such expenses pursuant to Internal Revenue Code ("IRC") Section 174. The capitalized expenses are amortized over a 5-year period for domestic expenses and a 15-year period for foreign expenses. As a result of this provision of the Tax Act, deferred tax assets related to capitalized research expenses increased by $21.4 million.

At December 31, 2022, the Company's federal and state income tax net operating loss carryforwards were approximately $369.9 million and $465.6 million, respectively, which may be subject to limitations as described below. If not utilized, the federal tax loss carryforwards will begin to expire in 2035 and the state tax loss carryforwards will begin to expire in 2035. Under the Tax Act, federal net operating losses generated after 2017 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. The federal net operating losses generated after December 31, 2017 of $319.3 million are carried forward indefinitely. In addition, the Company has certain federal, California and Massachusetts research and development income tax credit carryforwards of $13.7 million, $7.7 million and $1.5 million, respectively. If not utilized, the federal research and development income tax credit carryforwards will begin to expire in 2035. The California research and development income tax credit carryforwards do not expire and can be carried forward indefinitely. The Massachusetts research and development income tax credit carryforwards will begin to expire in 2035.

Net operating loss and tax credit carryforwards as of December 31, 2022 are as follows (in thousands):

	Amount	Expiration Years
Net operating losses, federal (post December 31, 2017)	$ 319,266	Do not expire
Net operating losses, federal (pre January 1, 2018)	50,587	2035 - 2037
Net operating loss, state	465,623	2035 - 2042
Tax credits, federal	13,669	2035 - 2042
Tax credits, state	9,160	CA: credits do not expire MA: 2035 - 2042

The net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under IRC Sections 382 and 383. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. Subsequent ownership

changes may further affect the limitation in future years. In connection with the Company's IPO, which closed in October 2018, the Company did experience an ownership change pursuant to Section 382. There was no reduction in federal or California net operating loss carryforwards or research and development income tax credits as a result of this ownership change. The Company is in the process of completing an analysis through December 31, 2022 under IRC Sections 382 and 383 to determine if the Company's net operating loss carryforwards and research and development credits are limited due to a change in ownership and may have an ownership change pursuant to Section 382.

The following table summarizes the activity related to the Company's unrecognized tax benefits (in thousands):

	December 31,		
	2022	2021	2020
Beginning of year—unrecognized tax benefits	$ 5,481	$ 4,025	$ 2,610
Decrease for tax positions taken during prior periods	—	—	—
Increases for tax positions taken during current period	1,234	1,456	1,415
End of year—unrecognized tax benefits	$ 6,715	$ 5,481	$ 4,025

If recognized, none of the unrecognized tax benefits as of December 31, 2022, 2021, and 2020 would impact the annual effective tax rate, primarily due to corresponding adjustments to the valuation allowance. The Company does not expect any material changes to the estimated amount of liability associated with its uncertain tax positions within the next twelve (12) months.

During the years ended December 31, 2022, 2021, and 2020, the Company did not recognize accrued interest and penalties related to unrecognized tax benefits.

The Company files income tax returns in the U.S. federal jurisdiction and various state jurisdictions. The Company is not currently under audit by the Internal Revenue Service or other similar state or local authorities. Due to the net operating loss carryforwards, all years remain open for income tax examination by tax authorities in the United States and various state tax jurisdictions in which the Company files tax returns.

13. Net Loss Per Common Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents.

The following table sets forth the computation of the basic and diluted net loss per share (in thousands, except for share and per share amounts):

	Year Ended December 31,		
	2022	2021	2020
Numerator:			
Net loss	$ (119,687)	$ (75,082)	$ (105,314)
Denominator:			
Weighted-average common shares outstanding, basic and diluted	90,918,333	78,885,186	37,792,365
Net loss per share, basic and diluted	$ (1.32)	$ (0.95)	$ (2.79)

In December 2020, the Company issued and sold Warrants to purchase 27,480,719 shares of common stock at a nominal exercise price of $0.01 per share, and in October 2022 the Company issued and sold Warrants to purchase 13,274,923 shares of common stock at a nominal exercise price of $0.0001 per share (see Note 10). During the year ended December 31, 2022, 3,442,567 warrants were exercised, resulting in the Company issuing 3,442,567 shares of common stock. During the year ended December 31, 2021, there were 10,459,576 warrants exercised and 4,872 warrants cancelled due to net exercise of the warrants. As of December 31, 2022 and 2021, there are 26,848,627 and 17,016,271 warrants outstanding, respectively. The shares of common stock into which the Warrants may be exercised are considered outstanding for the purposes of computing earnings per share, because the shares may be issued for little or no consideration, they are fully vested and they are immediately exercisable upon their issuance date.

During a period of net loss, basic net loss per share is the same as diluted net loss per share, as the inclusion of all potential common shares outstanding would have been anti-dilutive. Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	December 31,		
	2022	2021	2020
Options issued and outstanding and ESPP shares issuable and outstanding	7,145,817	5,170,331	4,213,738
Restricted stock subject to future vesting	561,526	708,800	—
Total	7,707,343	5,879,131	4,213,738

14. Defined Contribution Plan

The Company began sponsoring a 401(k) Plan in 2017, which provides that eligible employees can elect to contribute to the 401(k) Plan, subject to certain limitations, on a pretax basis. The Company matches up to 50% of the first 4% of each employee's contribution. During the years ended December 31, 2022 and 2021, expenses recognized for the 401(k) Plan was $0.5 million and $0.4 million, respectively, while the amount was immaterial for the year ended December 31, 2020.

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

None.

Item 9A. Controls and Procedures.

Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures

As of December 31, 2022, management, with the participation of our principal executive, financial and accounting officers, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including the principal executive, financial and accounting officers, to allow timely decisions regarding required disclosures.

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

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the year ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act). Under the supervision of and with the participation of our Principal Executive Officer and our Principal Financial Officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in "Internal Control-Integrated Framework" (2013). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2022.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm on our internal control over financial reporting due to an exemption established by the JOBS Act for "emerging growth companies."

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers, employees and consultants. The Code of Business Conduct and Ethics is available on the Corporate Governance page of our website at www.gritstonebio.com. If we ever were to amend or waive any provision of our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer, controller or any person performing similar functions, we intend to satisfy our disclosure obligations with respect to any such waiver or amendment by posting such information on our internet website set forth above rather than filing a Form 8-K.

All other information required by this item will be contained in our definitive proxy statement to be filed with the SEC on Schedule 14A in connection with our 2023 Annual Meeting of Stockholders (the "Proxy Statement"), which is expected to be filed not later than 120 days after December 31, 2022, and is incorporated herein by reference.

Item 11. Executive Compensation.

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

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

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

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

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

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

1. Financial Statements

See Index to Financial Statements in Part II Item 8 of this Annual Report on Form 10-K.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits

The documents listed in the Exhibit Index are incorporated by reference or are filed with this report, in each case as indicated therein (numbered in accordance with Item 601 of Regulation S-K).

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1(a)	Amended and Restated Certificate of Incorporation.	8-K	10/02/18	3.1	
3.1(b)	Certificate of Amendment to Amendment and Restated Certificate of Incorporation.	8-K	05/06/21	3.1	
3.2	Amended and Restated Bylaws.	8-K	10/02/18	3.2	
4.1	Reference is made to exhibits 3.1 through 3.2.				
4.2	Form of Common Stock Certificate.	S-1/A	09/17/18	4.2	
4.3	Description of Common Stock.	10-K	03/10/22	4.3	
4.4	Form of Pre-Funded Warrant issued in First PIPE Financing.	10-K	12/28/20	4.1	
4.5	Form of Pre-Funded Warrant issued in Third PIPE Financing.	8-K	10/25/2022	4.1	
10.1(a)†	License Agreement, dated as of October 16, 2017, by and among Gritstone Oncology, Inc., Arbutus Biopharma Corporation and its subsidiary Protiva Biotherapeutics Inc.	S-1	08/23/18	10.1 (a)	
10.1(b)†	Amendment Number One to License Agreement, dated as of July 20, 2018, by and among Gritstone Oncology, Inc., Arbutus Biopharma Corporation and its subsidiary Protiva Biotherapeutics Inc.	S-1	08/23/18	10.1 (b)	
10.2	Collaboration, Option and License Agreement by and between Gilead Sciences, Inc. and Gritstone Oncology, Inc., dated as of January 29, 2021.	10-K	03/10/22	10.3	
10.3(a)#	2018 Incentive Award Plan.	S-8	10/02/18	99.2 (A)	
10.3(b)#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2018 Incentive Award Plan.	S-1/A	09/17/18	10.7 (b)	
10.3(c)#	Form of Restricted Stock Award Grant Notice under the 2018 Incentive Award Plan.	S-1/A	09/17/18	10.7 (c)	
10.3(d)#	Form of Restricted Stock Unit Award Grant Notice under the 2018 Incentive Award Plan.	S-1/A	09/17/18	10.7 (d)	
10.4(a)#	2021 Employment Inducement Incentive Plan.	S-8	05/06/21	99.1	
10.4(b)#	Form of Stock Option Agreement under the 2021 Employment Inducement Incentive Plan.	S-8	05/06/21	99.2	
10.4(c)#	Form of Restricted Stock Unit Award Agreement under the 2021 Employment Inducement Incentive Plan.	S-8	05/06/21	99.3	
10.4(d)#	Form of Stock Award Agreement under the 2021 Employment Inducement Incentive Plan.	S-8	05/06/21	99.4	

10.5#	Employment Agreement by and between Gritstone Oncology, Inc. and Andrew Allen, M.D., Ph.D., effective as of September 27, 2018.	S-1/A	09/17/18	10.9	
10.6#	Employment Agreement by and between Gritstone Oncology, Inc. and Matthew Hawryluk, Ph.D., effective as of September 27, 2018.	S-1/A	09/17/18	10.10	
10.7#	Employment Agreement by and between Gritstone Oncology, Inc. and Karin Jooss, Ph.D., effective as of September 27, 2018.	S-1/A	09/17/18	10.11	
10.8#	Employment Agreement by and between Gritstone Oncology, Inc. and Erin Jones, effective as of September 27, 2018.	S-1/A	09/17/18	10.16	
10.9#	Employment Agreement by and between Gritstone bio, Inc., and Vassiliki Economides, effective as of June 23, 2021.	10-K	03/10/22	10.10	
10.10#	Amended and Restated Non-Employee Director Compensation Program.	10-K	03/10/22	10.11	
10.11#	2018 Employee Stock Purchase Plan.	S-8	10/02/18	99.3	
10.12	Lease, dated as of February 11, 2016, by and between Gritstone Oncology, Inc. and BMR-Sidney Research Campus LLC.	S-1	08/23/18	10.4	
10.13	Office Building Net Lease, dated as of March 24, 2017, by and between Gritstone Oncology, Inc. and Hacienda Portfolio Venture, LLC.	S-1	08/23/18	10.5	
10.14	Office/Laboratory Lease, by and between Gritstone Oncology, Inc. and Emery Station West, LLC, effective as of January 28, 2019.	8-K	02/05/19	10.1	
10.15	Office/Laboratory Lease, by and between Gritstone Oncology, Inc. and MIL 21E, LLC, effective as of September 6, 2018.	10-Q	11/20/19	10.2	
10.16	First Amendment to Office/Laboratory Lease, by and between Gritstone Oncology, Inc. and MIL 21E, LLC, effective as of July 11, 2019.	10-Q	11/20/19	10.3	
10.17	Second Amendment to Office/Laboratory Lease, by and between Gritstone Oncology, Inc. and MIL 21E, LLC, effective as of May 20, 2020.	10-Q	08/05/20	10.1	
10.18	Office/Laboratory Lease, by and between Gritstone bio, Inc. and RREF II Kenmore Lessor III LLC and RREF II Kenmore Lessor IV LLC, effective as of September 23, 2021.	8-K	09/29/21	10.1	
10.19	First Amendment to Lease, by and between Gritstone bio, Inc. and MIL 21E, LLC, effective as of September 21, 2021.	8-K	09/29/21	10.2	
10.20	Third Amendment to Office/Laboratory Lease, by and between Gritstone bio, Inc. and MIL 21E, LLC, effective as of September 21, 2021.	8-K	09/29/21	10.3	
10.21	Fourth Amendment to License Agreement between Gritstone bio, Inc. and MIL 21E LLC, effective as of June 6, 2022.	10-Q	08/04/22	10.1	
10.22	Fifth Amendment to License Agreement between Gritstone bio, Inc. and MIL 21E LLC effective, effective as of June 13, 2022.				X
10.23	Form of Indemnification Agreement.	S-1/A	09/17/18	10.18	
10.24	Securities Purchase Agreement, dated December 22, 2020.	8-K	12/28/20	10.1	
10.25	Securities Purchase Agreement, dated December 28, 2020.	8-K	12/30/20	10.1	
10.26	Loan and Security Agreement between the Company, Hercules Capital, Inc. and Silicon Valley Bank and certain other parties thereto, dated as of July 19, 2022.	10-Q	11/03/22	10.1	
23.1	Consent of Independent Registered Public Accounting Firm				X
31.1	Certification of Chief Executive Officer, as required by Rule 13a-14(a) or Rule 15d-14(a) under the Securities Exchange Act of 1934, as amended.				X
31.2	Certification of Chief Financial Officer, as required by Rule 13a-14(a) or Rule 15d-14(a) under the Securities Exchange Act of 1934, as amended.				X

32*	Certification by the Chief Executive Officer and Chief Financial Officer, as required by Rule 13a-14(b) or Rule 15d-14(b) under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 36 of Title 18 of the United States Code (18 U.S.C. §1350).	X
101.INS	Inline XBRL Instance Document	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document	X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X
104	The cover page from the Company's Annual Report on Form 10-K for the year ended December 31, 20221 has been formatted in Inline XBRL.	X

† Confidential treatment has been granted for certain information contained in this exhibit. Such information has been omitted and filed separately with the SEC.

# Indicates management contract or compensatory plan.

* The certification attached as Exhibit 32 that accompanies this Annual Report on Form 10-K is not deemed filed with the SEC and is not to be incorporated by reference into any filing of Gritstone bio, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized**.**

GRITSTONE BIO, INC.

Date: March 9, 2023

By: /s/ Andrew Allen
Andrew Allen, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints each of Andrew Allen and Vassiliki Economides his or her true and lawful attorney-in-fact and agent, with full power of substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the U.S. Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents, or their, his or her substitutes or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Andrew Allen Andrew Allen, M.D., Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 9, 2023
/s/ Vassiliki “Celia” Economides Vassiliki “Celia” Economides	Chief Financial Officer (Principal Financial Officer)	March 9, 2023
/s/ James Cho James Cho	Chief Accounting Officer (Principal Accounting Officer)	March 9, 2023
/s/ Elaine Jones Elaine Jones, Ph.D.	Chairperson of our Board of Directors	March 9, 2023
/s/ Clare Fisher Clare Fisher	Director	March 9, 2023
/s/ Steve Krognes Steve Krognes	Director	March 9, 2023
/s/ Naiyer A. Rizvi Naiyer A. Rizvi, M.D.	Director	March 9, 2023
/s/ Lawrence Corey Lawrence Corey, M.D.	Director	March 9, 2023
/s/ Shefali Agarwal Shefali Agarwal, M.D., M.P.H.	Director	March 9, 2023

Exhibit 10.22

Fifth Amendment to License Agreement

This Fifth Amendment to License Agreement ("**Fifth Amendment**") is dated June 13, 2022 ("**Effective Date**") and entered into by and between Gritstone bio, Inc., formerly known as Gritstone Oncology, Inc. ("**Licensee**") and MIL 21E, LLC ("**Licensor**").

WHEREAS, Licensor and Licensee are parties to a certain License Agreement dated September 6, 2018, as amended by that certain First Amendment to License Agreement dated July 11, 2019, as amended by that certain Second Amendment to License Agreement dated May 20, 2020, as amended by that certain Third Amendment to License Agreement dated September 21, 2021 as amended by that certain Fourth Amendment to License Agreement dated June 6, 2022 (collectively, "**License Agreement**");

WHEREAS, Licensee warrants and represents that, to the best of its knowledge, Licensor has fulfilled its obligations under the License Agreement and is not in default of any covenants or obligations contained in the License Agreement;

WHEREAS, Licensor and Licensee desire to amend the License Agreement in certain respects as set forth herein; and,

WHEREAS, all capitalized terms contained herein shall, unless otherwise defined in this Fifth Amendment, have the same meaning as set forth in the License Agreement.

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties agree that the License Agreement agree as follows:

1. Parking. The License Agreement is hereby amended by adding the following language to the end of Section 6:

   Subject to ongoing availability, Licensee shall have a non-exclusive, revocable license to use one (1) additional unreserved parking space ("**Additional Parking Space**"). Licensee shall be responsible for the Additional Parking Space Fee (defined below) for such space regardless of whether its Occupants use the Additional Parking Space. Licensee shall pay, in addition to the License Fee and Parking Fees, a monthly parking fees equal to the prevailing rate for the Additional Parking Space ("**Additional Parking Space Fees**") and shall pay such Additional Parking Space Fees to SmartLabs at the time each License Fee payment is due.

2. Ratification. Except as amended herein, all terms and conditions of the License Agreement shall remain unchanged and in full force and effect.

3. Counterparts. This Fifth Amendment to License Agreement may be executed in any number of counterparts, each of which shall be an original and all of which together shall constitute one and the same document.

[signatures on following page]

IN WITNESS WHEREOF, Licensor and Licensee have duly executed this Fifth Amendment as of the Effective Date.

LICENSOR

/s/ Brian Taylor

By: Brian Taylor
Title: Head of Field Operations

LICENSEE

/s/ Erin Jones

By: Erin Jones
Title: Chief Operating Officer

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Form S-3 Nos. 333-234211, 333-252564, 333-260292, 333-263455, and 333-268524) and related Prospectuses of Gritstone bio, Inc. (f/k/a Gritstone Oncology, Inc.),

(2) Registration Statements (Form S-8 Nos. 333-230581, 333-237095, 333-254177, 333-255847, 333-263451 and 333-264804) pertaining to the 2018 Incentive Award Plan, the 2018 Employee Stock Purchase Plan, and the 2021 Employment Inducement Incentive Plan, in each case, of Gritstone bio, Inc. (f/k/a Gritstone Oncology, Inc.), and

(3) Registration Statement (Form S-8 No. 333-227665) pertaining to the 2015 Equity Incentive Plan, the 2018 Incentive Award Plan and the 2018 Employee Stock Purchase Plan, in each case, of Gritstone bio, Inc. (f/k/a Gritstone Oncology, Inc.)

of our report dated March 9, 2023, with respect to the consolidated financial statements of Gritstone bio, Inc. included in this Annual Report (Form 10-K) of Gritstone bio, Inc. for the year ended December 31, 2022.

/s/ Ernst & Young LLP

San Mateo, California
March 9, 2023

Exhibit 31.1

CERTIFICATION OF PRESIDENT AND CHIEF EXECUTIVE OFFICER PURSUANT TO EXCHANGE ACT RULES 13A-14(A) AND 15D-14(A), AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Andrew Allen, M.D., Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Gritstone bio, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 9, 2023

By: /s/ Andrew Allen

Andrew Allen, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER PURSUANT TO EXCHANGE ACT RULES 13A-14(A) AND 15D-14(A), AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Vassiliki Economides, certify that:

1. I have reviewed this Annual Report on Form 10-K of Gritstone bio, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 9, 2023

By:

/s/ Vassiliki Economides

Vassiliki Economides
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Gritstone bio, Inc. (the "Company") for the period ended December 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of Andrew Allen, M.D., Ph.D., President and Chief Executive Officer (Principal Executive Officer) of the Company, and Vassiliki Economides, Chief Financial Officer (Principal Financial Officer) of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 9, 2023

/s/ Andrew Allen

Andrew Allen, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: March 9, 2023

/s/ Vassiliki Economides

Vassiliki Economides
Chief Financial Officer
(Principal Accounting Officer)