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, 2021

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 001-39103

CABALETTA BIO, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**82-1685768**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
2929 Arch Street, Suite 600 Philadelphia, PA	**19104**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (267) 759-3100

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, par value $0.00001 per share	CABA	The Nasdaq Global Select Market

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

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

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

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

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

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

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

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

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

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

As of June 30, 2021 (the last business day of the registrant's most recently completed second fiscal quarter), the aggregate market value of the registrant's common stock held by non-affiliates was approximately $205 million based on the last reported sale price of the registrant's common stock on the Nasdaq Global Select Market on June 30, 2021.

The number of shares of registrant's Common Stock outstanding as of March 10, 2022 was 28,977,129.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates by reference certain information from the registrant's definitive Proxy Statement for its 2022 annual meeting of shareholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year end of December 31, 2021. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

Table of Contents

		Page
PART I		3
Item 1.	Business	3
Item 1A.	Risk Factors	55
Item 1B.	Unresolved Staff Comments	118
Item 2.	Properties	118
Item 3.	Legal Proceedings	118
Item 4.	Mine Safety Disclosures	118
PART II		119
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	119
Item 6.	Reserved	119
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	120
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	132
Item 8.	Financial Statements and Supplementary Data	132
Item 9.	Changes in and Disagreements With Accountants on Accounting and Financial Disclosure	132
Item 9A.	Controls and Procedures	133
Item 9B.	Other Information	134
Item 9C.	Disclosure Regarding Foreign Jurisdictions that Prevent Inspections	134
PART III		135
Item 10.	Directors, Executive Officers and Corporate Governance	135
Item 11.	Executive Compensation	135
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	135
Item 13.	Certain Relationships and Related Transactions, and Director Independence	135
Item 14.	Principal Accounting Fees and Services	135
PART IV		136
Item 15.	Exhibits, Financial Statement Schedules	136
Item 16	Form 10-K Summary	136
	Signatures	141

Summary of the Material and Other Risks Associated with Our Business

- We are a clinical-stage company with a limited operating history, have incurred significant losses since our inception, and anticipate that we will continue to incur significant losses for the foreseeable future.
- We are highly dependent on our relationship with University of Pennsylvania, or Penn, for our preclinical research and development activities, key technology and our current manufacturing needs for our clinical trial of DSG3-CAART, or the DesCAARTes™ trial, and if Penn's manufacturing capacity is reduced or otherwise delayed or limited, this could adversely impact enrollment in our DesCAARTes™ trial.
- We are reliant on intellectual property licensed to us by Penn and termination of our license agreement with Penn would result in the loss of significant rights, which would have a material adverse effect on our business.
- If we are unable to obtain and maintain sufficient intellectual property protection for DSG3-CAART, our other product candidates and technologies or any future product candidates, we may not be able to compete effectively in our markets.
- We will need to raise substantial additional funding before we can expect to complete development of any of our product candidates or generate any revenues from product sales.
- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- If we are unable to successfully develop our current programs into a portfolio of product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our current and future product candidates.
- If we encounter difficulties enrolling patients in our DesCAARTes™ trial, our planned Phase 1 clinical trial for MuSK-CAART, or the MusCAARTes™ trial, or future clinical trials, these clinical development activities could be delayed or otherwise adversely affected.
- If we are unable to advance our product candidates through clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.
- Results of earlier studies may not be predictive of future study or trial results, and we may fail to establish an adequate safety and efficacy profile to conduct clinical trials or obtain regulatory approval for our product candidates.
- If serious adverse events, undesirable side effects or unexpected characteristics are identified during the development of any of our product candidates, we may need to delay, abandon or limit our further clinical development of those product candidates.
- The ongoing coronavirus disease, or COVID-19, pandemic and the future outbreak of other highly infectious or contagious diseases could seriously harm our research, development and potential future commercialization efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.
- Manufacturing and administering our product candidates is complex and we may encounter difficulties in technology transfer from Penn to a contract manufacturing organization.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- We may establish our own manufacturing facility and infrastructure in addition to or in lieu of relying on third parties for the manufacture of our product candidates, which will be costly and time-consuming, and which may not be successful.
- Our future success depends in part upon our ability to retain our key employees, consultants and advisors and to attract, retain and motivate other qualified personnel.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, including the sections entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or 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. Forward-looking statements in this Annual Report on Form 10-K include, but are not limited to, statements about:

- the success, cost and timing and conduct of our clinical trial program, including our clinical trial of DSG3-CAART, or the DesCAARTes ™ trial, our planned Phase 1 clinical trial of MuSK-CAART, or the MusCAARTes™ trial, and our other product candidates, including statements regarding the timing of initiation and completion of the clinical trials and the period during which the results of the clinical trials will become available;
- the timing of and our ability to obtain and maintain regulatory approval of our product candidates, including DSG3-CAART, MuSK-CAART, FVIII-CAART, DSG3/1-CAART and PLA2R-CAART, in any of the indications for which we plan to develop them, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- the impact of any business interruptions to our operations, including the timing and enrollment of patients in our ongoing and planned clinical trials and our planned Investigational New Drug application submissions, or to those of our clinical sites, manufacturers, suppliers, or other vendors resulting from the COVID-19 pandemic or similar public health crisis;
- our expected use of proceeds from the initial public offering and from sales of our common stock in "at-the-market" offerings and the period over which such proceeds, together with existing cash, will be sufficient to meet our operating needs;
- our plans to pursue research and development of other product candidates;
- our plan to infuse our DSG3-CAART product candidate without lymphodepletion or other preconditioning agents initially in our DesCAARTes™ trial;
- the potential advantages of our proprietary Cabaletta Approach for selective B cell Ablation platform, called our CABA™ platform, and our product candidates;
- the extent to which our scientific approach and CABA™ platform may potentially address a broad range of diseases;
- the potential benefits and success of our arrangements and our expanded sponsored research agreement with the Trustees of the University of Pennsylvania, or Penn, and the Children's Hospital of Philadelphia, or CHOP, and our scientific co-founders, Drs. Milone and Payne;
- our ability to successfully commercialize our product candidates, including DSG3-CAART and our other product candidates;
- the potential receipt of revenue from future sales of DSG3-CAART and our other product candidates;
- the rate and degree of market acceptance and clinical utility of DSG3-CAART and our other product candidates;
- our estimates regarding the potential market opportunity for DSG3-CAART and our other product candidates, and our ability to serve those markets;
- our sales, marketing and distribution capabilities and strategy, whether alone or with potential future collaborators;
- our ability to establish and maintain arrangements or a facility for manufacture of DSG3-CAART and our other product candidates;
- our ability to obtain funding for our operations, including funding necessary to initiate and complete our DesCAARTes™ trial, our planned MusCAARTes™ trial, our ongoing preclinical studies of DSG3/1-CAART, FVIII-CAART and PLA2R-CAART;
- the potential achievement of milestones and receipt of payments under our collaborations;
- our ability to enter into additional collaborations with existing collaborators or other third parties;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates and our ability to operate our business without infringing on the intellectual property rights of others;
- the success of competing therapies that are or become available, and our competitive position;
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the impact of government laws and regulations in the United States and foreign countries; and
- our ability to attract and retain key scientific or management personnel.

These factors should not be construed as exhaustive and should be read in conjunction with the other cautionary statements that are included in this Annual Report on Form 10-K. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we undertake no obligations to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

PART I

Item 1. Business.

Overview

We are a clinical-stage biotechnology company focused on the discovery and development of engineered T cell therapies, and aim to provide a deep and durable, perhaps curative, treatment, for patients with B cell-mediated autoimmune diseases. Our proprietary technology utilizes Chimeric AutoAntibody Receptor, or CAAR, T cells that are designed to selectively bind and eliminate only specific B cells that produce disease-causing autoantibodies, or pathogenic B cells, while sparing normal B cells. Our lead CAAR T cell product candidate was designed based on the clinically validated and commercially approved Chimeric Antigen Receptor, or CAR, T cell technology that is marketed for the treatment of B cell cancers. By harnessing the power of targeted cell therapy, we believe our CAAR T product candidates have the potential to provide responses that may be a safer and more effective option than current treatments. We believe our technology, in combination with our proprietary Cabaletta Approach for selective B cell Ablation platform, called our CABA™ platform, has applicability across over two dozen B cell-mediated autoimmune diseases that we have identified, evaluated, and prioritized.

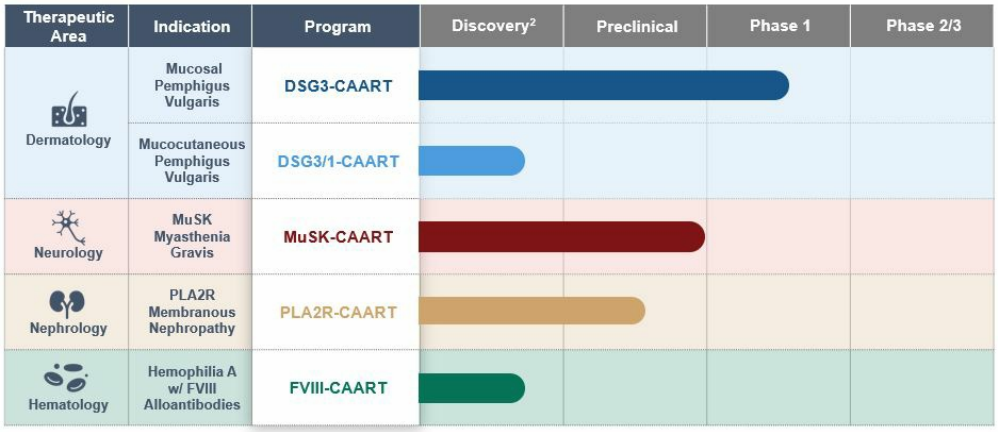
Our initial focus is mucosal pemphigus vulgaris, or mPV, which is an autoimmune blistering disease. Our lead product candidate, DSG3-CAART, is being evaluated for the treatment of mPV, a subtype of pemphigus vulgaris, or PV, that affects the mucous membrane. mPV is caused by autoantibodies against the cell adhesion protein desmoglein 3, or DSG3. DSG3-CAART is designed to selectively target and eliminate autoreactive B cells specific for DSG3, which may prevent these B cells from differentiating into antibody secreting plasma cells that produce anti-DSG3 antibodies that are the cause of mPV, while preserving general B cell immune function. DSG3-CAART is being evaluated in a Phase 1 trial, or the DesCAARTes ™ trial, in which we are currently enrolling patients. During 2021, we reported acute and 28-day safety data from the first three cohorts of patients in the DesCAARTes ™ trial, with no dose-limiting toxicities, or DLTs, or clinically relevant adverse events observed in the 28 days after infusion of DSG3-CAART. In November 2021, we reported that dose-dependent increases in DSG3-CAART persistence in the third cohort relative to the first two low dose cohorts throughout the 28 days following infusion had been observed. On December 14, 2021, we reported top-line biologic activity data for the first, two low dose cohorts, where no clear evidence of biologic activity was observed at doses that represent less than 2% of the current planned maximum dose in the trial, as well as the continued absence of any DLTs or clinically relevant adverse events. Furthermore, we announced the addition of a planned fifth cohort to receive a higher dose with a more consolidated dosing regimen, which we expect to initiate in 2022 after review of the fourth cohort's 28-day safety data. In January 2022, we announced that 28-day safety data for the fourth cohort was anticipated to be announced in the first quarter of 2022, and that other clinical data updates from the DesCAARTes ™ trial are expected to be provided at scientific meetings throughout 2022 and 2023 with biologic activity data for cohorts A3 and A4 expected to be announced in mid-2022. In March 2022, we disclosed 28-day safety data for the fourth cohort with no DLTs observed in any patient during the 28 days after infusion of DSG3-CAART. In addition, we disclosed that we are currently enrolling patients for the fifth cohort, and expect to announce the 28-day safety data for the fifth cohort at a scientific meeting in mid-2022, assuming no DLTs are observed during such cohort, that enrollment is uninterrupted and there are no delays due to COVID-19 resurgence.

Our MuSK-CAART product candidate is designed for the treatment of muscle-specific kinase, or MuSK, myasthenia gravis, or MG. In the fourth quarter of 2021, we submitted an Investigational New Drug, or IND, application for the first-in-human studies to the United States Food and Drug Administration, or FDA. This IND became effective in January 2022. In February 2022, MuSK-CAART received fast track designation from the FDA for improving activities of daily living and muscle strength in patients with MuSK antibody-positive myasthenia gravis. We plan to initiate the Phase 1 clinical trial for MuSK-CAART, or the MusCAARTes™ trial, in 2022. We are also advancing additional product candidates currently in discovery-stage or preclinical development for the treatment of mucocutaneous PV, or mcPV, PLA2R-associated membranous nephropathy, or PLA2R MN, and Hemophilia A with Factor VIII, or FVIII, alloantibodies, in addition to two undisclosed targets. We conducted a pre-IND interaction with the FDA to discuss the development path for PLA2R-CAART in the fourth quarter of 2021. Preclinical data demonstrating that PLA2R CAAR T cells specifically recognized and eliminated anti-PLA2R antibody-expressing B cells and that membrane proteome arrays screened with PLA2R-CAAR candidates did not identify off-target interaction was presented at the American Society of Nephrology Kidney Week in the fourth quarter of 2021.

B cell-mediated autoimmune diseases occur when autoreactive B cells differentiate into plasma cells that produce autoantibodies, which are directed against specific healthy tissue or cells in the body. The presence of autoantibodies can manifest in a variety of autoimmune diseases and result in the destruction of healthy tissue in the body. Current treatment options for B cell-mediated autoimmune diseases are generally limited to corticosteroids and other generalized immunosuppressants that offer only temporary disease suppression, may require chronic, in-hospital administration and are associated with potentially life-threatening side effects. We believe the ideal therapy for B cell-mediated autoimmune diseases would selectively and completely eliminate the pathogenic B cells while sparing the body's normal B cells.

We are pioneering the development of a new class of engineered T cell therapies that express CAARs to selectively engage and eliminate pathogenic B cells. Our CAARs build upon the scientific foundation of CARs, differing primarily in the use of the antigen rather than an antibody fragment, which enables the CAAR T cells to serve as a "decoy" for specific autoantibodies expressed on the surface of B cells. This allows these pathogenic B cells to engage with the CAAR T cells instead of benign antigens, resulting in their elimination. We have developed our CABA™ platform to inform product candidate development from scientific, clinical, and commercial assessment through CAAR design. Using our CABA™ platform, we have identified and thoroughly evaluated over two dozen B cell-mediated autoimmune diseases that we believe will be amenable to treatment with the Cabaletta approach and have advanced several of our highest priority targets into discovery and preclinical testing.

Our current product candidate pipeline[1] is illustrated below.



1. *Two additional undisclosed disease targets, currently in discovery stage, and part of our pipeline portfolio through our Sponsored Research Agreement with the University of Pennsylvania are not shown.*
2. *In our discovery stage, we perform epitope mapping and optimize CAAR construct and design.*

Our initial therapeutic focus is on pemphigus vulgaris, or PV, a chronic, autoimmune blistering skin disease. Despite a current standard of care that includes corticosteroids and adjunctive immunosuppressive agents, PV remains associated with frequent recurrences as well as substantial morbidity and mortality. Our lead product candidate, DSG3-CAART, is being evaluated for the treatment of mPV, a subtype of PV that affects the epithelium of the mucous membranes. mPV is caused by autoantibodies against DSG3. In January 2020, the FDA granted orphan drug designation to DSG3-CAART for the treatment of PV. In May 2020, DSG3-CAART received fast track designation from the FDA for improving healing of mucosal blisters in patients with mPV. DSG3-CAART is currently being evaluated in the DesCAARTes™ trial. Our next PV-directed product candidate, DSG3/1-CAART, is being designed to target B cells that differentiate into antibody secreting cells that produce autoantibodies against DSG3 and desmoglein 1, or DSG1. It is being developed for the treatment of mucocutaneous PV, or mcPV, another subtype of PV that affects both mucosal and skin surfaces and is caused by autoantibodies against DSG3 and DSG1, respectively.

Our second clinical product candidate, MuSK-CAART, is designed to treat a subset of patients with MG. MG is an autoimmune disease induced by autoantibodies targeting the neuromuscular junction, or NMJ, which can lead to life-threatening muscle weakness. Our product candidate targets autoreactive B cells that differentiate into antibody secreting cells that produce autoantibodies against a transmembrane protein, muscle-specific kinase, or MuSK, and is being developed for the treatment of MuSK MG. Data from our initial *in vitro* and *in vivo* studies of MuSK-CAART was presented at the American Academy of Neurology's Science Highlights Virtual Platform in May 2020. The efficacy and safety of MuSK CAAR T cells were investigated using *in vitro* cytotoxicity assays, *in vitro* screens for off-target toxicity, and a mouse model to evaluate the efficacy of human MuSK CAAR T cells against MuSK antibody-expressing B cells *in vivo*. In preclinical studies, MuSK CAAR T cells demonstrated *in vitro* cytotoxicity towards B cell lines expressing various anti-MuSK antibodies, but we did not observe any cytotoxicity when anti-MuSK antibodies were not expressed. In addition, MuSK CAAR T cells also targeted and eliminated a panel of B cells targeting different MuSK epitopes. In an *in vivo* mouse model, MuSK CAAR T cells, but not control CAAR T cells, showed biological activity by blocking the growth of B cell lines expressing anti-MuSK antibodies. Based in part on these results, in the fourth quarter of 2021, we submitted an IND application for the first-in-human studies of MuSK-CAART to the FDA. This IND became effective in January 2022. In February 2022, MuSK-CAART received fast track designation from the FDA for improving activities of daily living and muscle strength in patients with MuSK antibody-positive myasthenia gravis. We plan to initiate the MusCAARTes™ trial in 2022.

PLA2R-CAART is being developed to treat patients with PLA2R-assoicated membranous nephropathy, an autoimmune disease that is typically caused by production of autoantibodies directed to phospholipase A2 receptor (PLA2R), a single-pass transmembrane protein expressed in the glomerulus of the kidney.

We are also pursuing development of an additional product candidate, FVIII-CAART, which is being designed to treat a subset of patients with Hemophilia A, an X-linked bleeding disorder caused by mutations in the FVIII gene. While our CABA™ platform is primarily focused on the treatment of B cell-mediated autoimmune diseases, we believe our approach may be applicable in other instances where B cell antibody production is implicated in immune response to exogenous proteins, such as FVIII administration for the treatment of Hemophilia A. Some patients receiving repeated administrations of exogenous FVIII will have an immune system response to the exogenous antigens, known as an alloimmune response. This can result in significant unmet need as these patients may develop alloantibodies against the treatment, also known as inhibitors, neutralizing the therapeutic potential of FVIII. Patients with FVIII alloantibodies may often require high-dose FVIII, immune tolerance induction with FVIII, agents that mimic FVIII or plasmapheresis to remove the FVIII alloantibodies. FVIII-CAART leverages a CAAR designed to target B cells expressing alloantibodies against FVIII, and it is initially being developed as an adjunctive therapy for Hemophilia A patients who develop FVIII alloantibodies.

Our manufacturing strategy is comprised of three stages, designed to initially leverage the extensive early-stage manufacturing expertise of our academic partners while migrating to contract manufacturing organization, or CMO, partnerships and ultimately aiming to achieve full manufacturing independence. Stage 1 leverages the expertise in cell and vector manufacturing of our partners at the Children's Hospital of Philadelphia, or CHOP, and the University of Pennsylvania, or Penn. This stage included early development work, support of the DSG3-CAART IND, and cell and vector product manufacturing for our DesCAARTes™ trial. We believe these partnerships and use of these established facilities have allowed us to move efficiently into clinical trials, but are not sufficient to support a commercial license. Stage 2, which is ongoing, is designed to engage partners who are qualified for manufacturing of vectors at commercial grade and scale and who have experience with cell processing. In January 2021, we initiated a collaboration with WuXi Advanced Therapies, Inc. or WuXi, to serve as our cell processing manufacturing partner, and have completed enabling engineering runs in preparation for our planned MusCAARTes™ trial. In December 2021, we entered into a license and supply agreement with Oxford Biomedica (UK) Limited, or Oxford Biomedica, to supply lentiviral vector for the clinical and commercial development of our DSG3-CAART candidate. Contingent on sufficient clinical evidence from the DesCAARTes™ trial, we plan to advance the third stage of our manufacturing strategy which will include leasing, building, qualifying and operating our own manufacturing facility. We believe this additional stage will enable full control of product development and commercial supply for products arising from our CABA™ platform, enabling us to achieve continuous improvement of our product candidates. Our Chief Executive Officer and our President, Science and Technology, have both, in prior roles, built and led organizations that have constructed and commissioned cell therapy facilities which we hope will enable us to smoothly transition to stage 3 when feasible.

We plan to build upon our first mover advantage in the field of targeted cell therapy for B cell-mediated autoimmune diseases and further advance the discovery, development, and commercialization of our CAAR T portfolio. Our extensive translational and correlative sciences program has been designed to inform clinical observations from the DesCAARTes ™ trial in order to preserve and expand our industry leading insights into the impact of CAAR T therapies in patients. Our scientific founders are leading experts in B cell-mediated autoimmune diseases and CAR T technology, and we are led by an experienced team with demonstrated success in discovering, developing, manufacturing and evaluating novel cell therapy products in clinical trials. We have assembled a Scientific Advisory Board with relevant experience in discovery, clinical and regulatory science for autoimmunity and cell and gene therapy. In addition, we have partnered our discovery and initial development efforts with Penn, a pioneer in cell and gene therapy with a proven track record of expertise in the translational research, clinical development, and manufacturing of cell therapy products, in order to advance our lead product candidate in clinical trials along with our preclinical product candidates.

Our History and Team

Our scientific co-founders, Aimee Payne, M.D., Ph.D., and Michael Milone, M.D., Ph.D., began partnering at Penn in 2013 to combine Dr. Payne's expertise in B cell-mediated autoimmune diseases with Dr. Milone's deep and experienced insights into the design and implementation of CAR T products. Dr. Payne is a worldwide leader in characterizing B cell-mediated autoantibody repertoires in PV and other autoimmune diseases. Dr. Milone is a renowned scientist in CAR T therapy and was a co-inventor of and a key driver in the preclinical discovery and development efforts that yielded Kymriah, the first FDA-approved CAR T therapy for the treatment of B cell cancers. Dr. Payne's laboratory surmised that by incorporating an antigen instead of an antibody fragment as the extracellular domain of the CAAR, specific pathogenic B cells could be targeted. This resulted in a collaboration between the two investigators to apply the scientific foundation of CAR T technology as it has been advanced by Drs. Payne and Milone in order to address B cell-mediated autoimmune diseases.

Their first scientific publication, "Reengineering chimeric antigen receptor T cells for targeted therapy of autoimmune disease" (*Science*, July 2016), attracted the attention of a colleague, Steven Nichtberger, M.D., who is an adjunct professor at the Wharton School at the University of Pennsylvania, teaching a class on biotech company formation, financing and leadership in the Vagelos Life Sciences & Management Program. Additionally, Dr. Nichtberger has experience creating and building companies, including a novel cellular therapy company, which required transferring the technology from an academic institution, establishing a research and development organization, hiring of manufacturing and quality teams, creating novel manufacturing processes, reaching agreement with the FDA on novel clinical development pathways and constructing a commercial-scale Good Manufacturing Practices, or GMP, facility that manufactured autologous cell therapy products for clinical trials. In 2017, based on over a year of interaction and discussions regarding the optimal strategy to advance the scientific opportunity into a commercially developed product portfolio that could offer potentially curative treatment options to patients, Drs. Payne, Milone and Nichtberger decided to launch Cabaletta Bio.

The longstanding and highly productive partnership between our co-founders has been complemented by additional management experience that brings a successful history of translating academic cellular therapy research from Penn and elsewhere into commercially sponsored clinical trials and the establishment of a GMP manufacturing facility and organization. Gwendolyn Binder, Ph.D., our President, Science and Technology, was an early member of the Translational Research Program Operations team at Penn for over five years and participated in the submission and acceptance of multiple INDs for novel engineered T cell therapy products. As part of the cell therapy organization at Penn, Dr. Binder partnered with Dr. Milone and others to drive the IND-enabling translational studies that facilitated the initial CAR T clinical trial in B cell cancers at Penn. Dr. Binder also built and led a clinical stage biotechnology company's manufacturing operations and quality teams, including creation of a fully functioning commercial grade GMP facility. Dr. Binder also built the translational research program and ultimately led the company's research organization.

Our Research and Manufacturing Collaboration with Penn

Our CABA™ platform has already produced multiple product candidates through our sponsored research agreements, or SRAs, with Penn for the laboratories of our scientific co-founders, Drs. Payne and Milone. Our continuing relationship with our scientific co-founders provides important guidance and insights to us. Our contractual relationship with Penn through ongoing licensing and research arrangements also provides important services around manufacturing supply.

In May 2020 and October 2021, we amended and restated our worldwide license agreement with Penn to develop our CAAR T technology to treat B cell-mediated autoimmune and alloimmune diseases. This license agreement provides us with access to multiple patent families covering CAAR T therapy as applied to the field of B cell-mediated autoimmune and alloimmune diseases and to the robust intellectual property portfolio created by Penn under these SRAs in this field. See "—Our Material Agreements—Amended and Restated License Agreement with Penn."

Our ongoing collaboration with Penn is also based on a Master Translational Research Services Agreement, or the Services Agreement, that we entered into in October 2018, along with multiple additional agreements under the Services Agreement to engage and partner in individual Penn entities, including cell product manufacturing, correlative research, vector manufacturing, clinical trial operations and protocol development. In addition to the Services Agreement, we have agreements in place with various functional areas and centers that provide additional resources to Penn as well as contractual commitments from Penn with the goal of providing the capacity to manufacture our lead product candidate, DSG3-CAART. Penn has also agreed to manufacture vector product for use in our clinical trials. Penn's obligations are subject to certain limitations and termination rights. See "—Our Material Agreements—Master Translational Research Services Agreement with Penn".

We believe Penn is uniquely suited to be our partner in our efforts to develop product candidates leveraging our CAAR T technology based on a decade of experience, including manufacturing and clinical support for approximately a dozen active cell therapy clinical trials. The original manufacturing process for the first FDA-approved CAR T therapy was developed at Penn before being transferred to Novartis Pharmaceuticals Corporation during late-stage clinical trials. We are leveraging Penn's experience, validated standard operating procedures, manufacturing facilities and staffing to accelerate development efforts for our lead product candidate.

Our Strategy

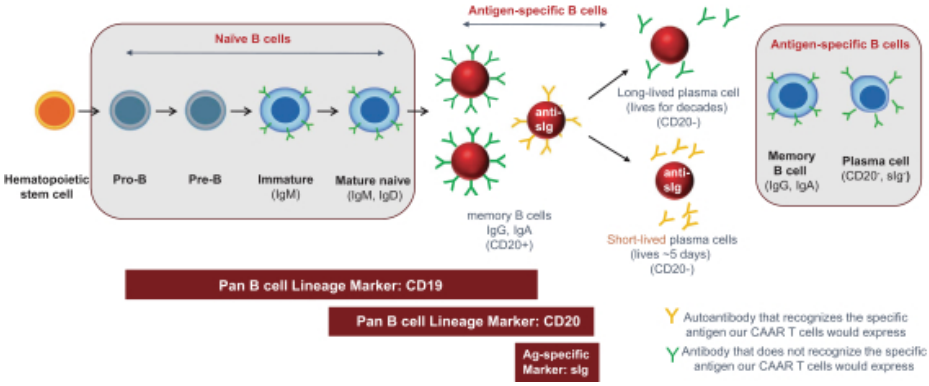
Our goal is to build upon our first mover advantage and expertise in cell therapies for B cell-mediated autoimmune diseases to accelerate the discovery, development and commercialization of our CAAR T cell therapies, with a focus on reliable manufacturing. We believe achieving this goal could result in potentially curative therapies for patients with unmet medical needs who suffer from certain B cell-mediated autoimmune diseases. To achieve this goal, key elements of our strategy include:

- ***Achieving clinical proof-of-concept for our lead product candidate, DSG3-CAART in mPV, the first in a series of well-understood and validated B cell-mediated autoimmune diseases for which we are developing CAAR T cell product candidates.*** It is well-established that the presence of DSG3 autoantibodies and DSG3 autoantibody producing cells in patients are both necessary and sufficient to cause mPV in the vast majority of cases. We believe our biologic understanding coupled with the well-understood clinical signs, symptoms and natural course of the disease, identify mPV as a model disease to evaluate our CAAR T approach. In addition, we have made significant investment in the design and development of DSG3-CAART, generating a lead candidate that has demonstrated robust target engagement and no off-target toxicities in preclinical studies. Taken together, our Phase 1 clinical trial evaluating DSG3-CAART for the treatment of mPV represents an optimal first opportunity to establish initial clinical proof-of-concept of our CABA™ platform.

- ***Leveraging our CABA™ platform to identify optimal targets for the CAAR T approach and apply learnings from DSG3-CAART to advance additional product candidates.*** Shortly after inception, we undertook a comprehensive review of all known B cell-mediated autoimmune diseases in order to evaluate and prioritize the opportunity for selective destruction of B cells in an effort to cure B cell-mediated autoimmune diseases. Central to this analysis were (i) scientific, clinical and commercial assessment, (ii) epitope mapping to determine regions targeted by autoantibodies, (iii) evaluation of the ability to optimize the CAAR construct and design with the goal of selectively ablating autoreactive B cells, and (iv) evaluation of existing or required development of new preclinical models and *in vitro* and *in vivo* clinical testing. As we performed this analysis of potential product candidates, we considered possible paths for clinical trial design and regulatory approval. This analysis incorporated the extensive learnings gleaned from years of effort devoted to development of DSG3-CAART. We prioritized the targets and since then have been focused on being first to discover and develop a series of products with each providing the potential for cure of an important B cell-mediated autoimmune disease in patients. We intend to continue to apply our proprietary learnings from DSG3-CAART, including scientific and regulatory learnings, to most effectively advance these additional opportunities. Preclinical studies that are generally similar to, and informed by, DSG3-CAART preclinical studies are actively ongoing with other CAAR T cell product candidates.
- ***Expanding upon our established IP position and first mover advantage in CAAR T therapy targeted towards B cell-mediated autoimmune diseases*** We are focused on protecting our intellectual property as we continue to pursue the development of future product candidates. We believe the issued U.S. patent on our initial CAAR constructs is the first patent covering cells engineered to express the known pathogenic epitopes recognized by DSG3 and DSG1 autoantibodies, which we are working to supplement with additional patent filings. The design of a broadly effective CAAR requires a deep understanding of the location of immunogenic epitopes targeted by autoantibodies, a competency that we believe we are uniquely positioned to utilize in product candidate development. We believe there is a particularly high value to the first mover advantage including, but not limited to, experience in discovery, preclinical development, regulatory efforts, intellectual property and insights from clinical trials that can be translated across programs.
- ***Leveraging our cellular therapy experience and knowledge in addition to knowledge gained through our Penn collaboration to rapidly build our own fully-integrated internal infrastructure.*** We have differentiated expertise that we believe is uniquely suited for the continued buildout of our CABA™ platform specializing in B cell-mediated autoimmune diseases. Our scientific co-founders who initially developed our technology continue to collaborate closely with us through SRAs. In addition, our management team has a successful history of building the capabilities of cell therapy-based companies from the discovery and preclinical stage through Phase 3 readiness. In combination with our team, which possesses significant experience in executing on manufacturing strategies for cell therapy products, our partnership with Penn allows us to utilize their existing infrastructure, which accelerated our ability to submit our first IND. In parallel, we continue to build out an experienced team to manage the relationship with Penn while also developing and continuing to implement a path to our manufacturing independence. Ultimately, we intend to prepare and build our own manufacturing facility depending on the achievement of sufficient initial clinical trial data for DSG3-CAART.

B Cell-Mediated Autoimmune Diseases: Overview and Current Treatment Paradigm

The body's immune system, which is designed to protect the body from infection and cancer, includes B cells and T cells. B cells are responsible for producing antibodies against antigens that the body perceives as foreign whereas T cells are responsible for cell-mediated immunity. In the case of B cell-mediated autoimmune diseases, certain populations of the patient's B cells differentiate into antibody secreting cells that produce antibodies directed against normal tissues and cells, leading to disease. While these autoantibodies are the major effectors of B cell-mediated autoimmune diseases, the underlying root cause of each B cell-mediated autoimmune disease is the defective B cells that mistakenly differentiate into cells that secrete these pathogenic antibodies. These pathogenic B cells express autoantibodies on their surface with the same antigen specificity as the circulating pathogenic autoantibodies, which can be used to distinguish them from the healthy B cell population, as shown in the figure below.



Antibodies are B cell receptors that drive B cell maturation. *CD19 serves as a B cell marker throughout the naïve B cell phase, while CD20 is a surface marker expressed later in B cell maturation. CAAR T is designed to eliminate antigen specific B cells and prevent their further development to antibody secreting plasma cells. IgM: immunoglobulin M; IgD: immunoglobulin D; IgA: immunoglobulin A; sIg: surface immunoglobulin, representing the autoantibody on the B cell surface.*

Current treatment options for autoimmune mediated diseases involve generalized immune suppression, achieved through corticosteroids, immunosuppressive medications and biologics. Most commonly, corticosteroids are used on both a chronic and acute basis to control disease, and act via a variety of mechanisms to control or downregulate multiple inflammatory pathways. In many cases, systemic immunosuppressive medications often used in chemotherapy such as mycophenolate, azathioprine and methotrexate, are added in an effort to minimize symptoms and manage the expected recurrences in patients. Biologic therapies have emerged as a new class of therapies and have a variety of targets including cytokines, B cells, and co-stimulation molecules. One particular biologic, rituximab, is an anti-CD20 antibody and is employed in multiple autoimmune diseases. Rituximab was approved by the FDA in 2018 for treatment of moderate to severe PV. Currently existing treatment options target parts of the immune system in addition to disease-causing B cells, and in general require chronic administration to reduce recurrence rates. We believe the ideal therapy in autoimmune diseases would completely and specifically eliminate the pathogenic B cells while sparing the immune cells that protect against infection, without requiring chronic administration.

Our Approach

Using our CABA™ platform, we are developing engineered T cell therapy candidates that express CAARs, which serve as "decoys" for antibodies expressed on the surface of B cells. We believe these CAARs enable the T cells to specifically engage and eliminate pathogenic B cells while sparing normal B cells. By harnessing the power of cell therapy, our technology has the potential to overcome the ability of these B cells to evade elimination and thus lead to durable responses. Our CAAR T platform is based on the foundation of established CAR T therapeutics, differing primarily in their use of the antigen rather than an antibody fragment to target pathogenic B cells. We believe our technology has broad applicability and we are building a portfolio of product candidates for B cell-mediated autoimmune diseases.

Background: CAR T Cells

Engineered T cell therapy is a type of immunotherapy in which human T cells are genetically modified to express specific receptors, enabling the T cells to recognize and eliminate pathogenic cells.

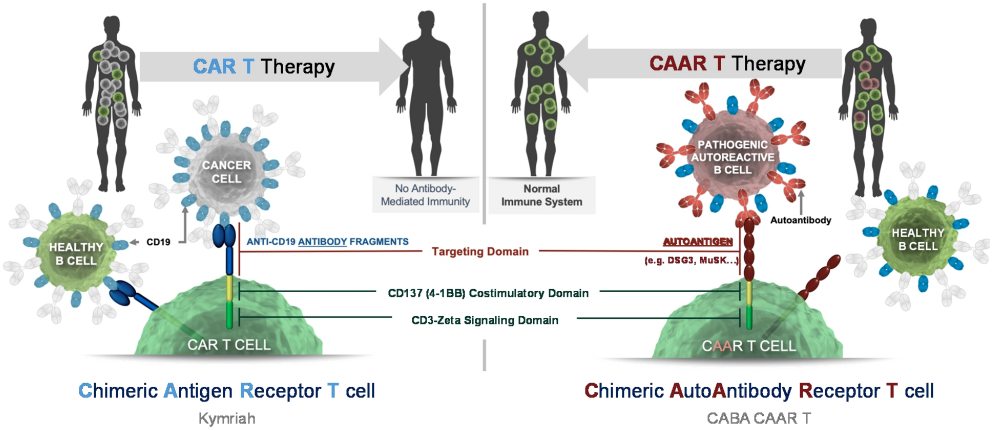
A key application of engineered cell therapy involves the use of CARs, which are engineered molecules that enable T cells to identify specific antigens present on the surface of diseased cells. When expressed on the patient's T cells, the CAR directs the T cells to kill cells that express a particular antigen. These CAR-expressing T cells, or CAR T cells, can proliferate, generating memory CAR T cells.

Many companies are using CAR T technology to develop therapies for the treatment of B cell cancers. Several drug candidates have demonstrated clinical success, leading to the first FDA regulatory approvals of CAR T therapies for certain B cell cancers. In these B cell cancers, CAR T therapy has resulted in complete remission of disease in many patients, even in cancer patients with severe, refractory disease. Despite success in treating certain B cell cancers, we believe that CARs have not yet been developed or evaluated as a treatment option for other types of B cell-mediated autoimmune diseases in patients.

Our Technology: CAARs

Our CAAR T platform builds upon the scientific foundation of CARs to enable targeted B cell elimination in an autoimmune setting, which may lead to complete and durable remission of disease while sparing all other B cell populations that can provide beneficial immunity from infection.

The co-stimulatory domain and the signaling domain of both a CAR T cell and CAAR T cell carry out the same activation and cytotoxic functions once the engineered cell therapy engages a B cell. Our CAAR T cells differ from CAR T cells primarily in the extracellular targeting domain. Our CAAR T cells incorporate the relevant parts of the autoantigen that is subject to attack in autoimmune disease, as shown in the figure below.



Key differences between CAR T (left) vs. CAAR T therapy (right) *A CAR T cell typically contains a signaling domain and a co-stimulatory domain and incorporates antibody fragments that recognize a specific antigen, such as CD19, which is present in both B cell leukemia cells and healthy B cells. In contrast, a CAAR T cell typically contains an antigen as its targeting domain rather than an antibody fragment. The antigen is recognized by the specific, pathogenic antibody along with the limited population of B cells that produce the antibody. The model CAAR T cell depicted here contains an identical signaling domain and a co-stimulatory domain. The primary difference between a CAR T cell and a CAAR T cell is the target domain expressed on the cell surface. The example shown demonstrates the pan-B cell ablation that happens when targeting the B cell lineage marker, CD19, and the highly selective pathogenic B cell targeting approach of CAAR T.*

Potential Advantages of CAAR T Cell Therapy in B Cell-Mediated Autoimmune Diseases

In contrast to currently available therapies for B cell-mediated autoimmune diseases, based on observations of CAR T activity in refractory B cell cancers, we believe a single CAAR T treatment could potentially offer complete and durable remission of certain specific B cell-mediated autoimmune diseases while leaving the humoral, or bodily fluid, antibody-producing immune system intact. We believe our CAAR T cells can recognize the specific autoantibodies that are responsible for causing an underlying disease and kill the cells that express the autoantibodies on their surface. As a result, we believe CAAR T cell therapy used in B cell-mediated autoimmune disease has the potential for durable elimination of pathogenic B cells and an associated elimination of clinical recurrences with an improved adverse event, or tolerability, profile relative to the current standard of care.

Enhanced target specificity and preservation of humoral immune system

Preservation of the humoral immune system with CAAR T cell therapy represents a potentially meaningful benefit over existing CD19- or CD20-targeting methods for B cell ablation, as patients would be less susceptible to infection they may encounter after non-specific B cell elimination and would not require chronic in-hospital treatment with intravenous immunoglobulin, or IVIG, or other prophylactic therapies. Additionally, because self-reactive B cells make up only 0.01% to 1% of the normal B cell population, we believe the risk of on-target toxicity may be reduced compared to systemically immunosuppressive medications that non-specifically weaken the immune system. Continued use of these drugs poses significant risks, such as the potential for fatal infections due to the non-specific tempering of the immune system related to the complete depletion of CD20+ or CD19+ B cells.

Potential for complete, long-lasting elimination of pathogenic B cells

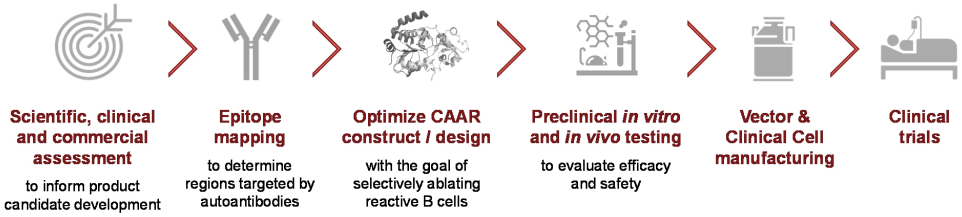
The current standard of care for B cell-mediated autoimmune disease displays limited and transient therapeutic benefit while also weakening the humoral immune system. We believe our CAAR T cells have the potential to eliminate the reactive, antibody-producing B cells that are ultimately responsible for disease, while sparing normal B cells. The curative potential of CAAR T cells would be consistent with clinical findings from use of CAR T products in B cell cancers and would be a significant improvement relative to the current standard of care for certain B cell-mediated autoimmune diseases.

While CAR T has demonstrated significant clinical success in B cell cancers, cancer cells employ a variety of mechanisms to evade detection by targeting immune cells, and antigen escape poses a significant risk of failure for CAR T cell treatment in oncology. Antigen escape in CAR T treatment occurs when the antigen that the CAR T cell targets is lost from or mutated within the malignant cell. Clinically, this results in response rates that decline from an initial complete response level of about 80% to approximately 50% over a period of years.

We believe this risk of antigen escape is reduced in our setting as mechanisms to evade CAAR T therapy would involve B cell receptor down-regulation or mutation such that antigen specificity is lost. We believe that the implication of this is that the mutated B cell would no longer produce autoantibodies that recognize the antigen and therefore should no longer be pathogenic. We also believe that a single infusion of CAAR T cells has the potential for curative effects due to either complete ablation of pathogenic cells or production of memory CAAR T cells.

Our CABA™ Platform

Our team has developed our CABA™ platform to inform product candidate development from indication selection through preclinical studies. Using our CABA™ platform, our team has identified our highest priority target indications following a rigorous analysis of B cell-mediated autoimmune diseases. A deep understanding of the antigenic epitopes targeted in these diseases is required to design and construct a successful CAAR. Our scientific founders have studied B cell repertoires for many years in the context of PV. Their expertise is essential to provide insights and guidance regarding our portfolio of products. We leverage the experience and insight gained from the development of each product candidate to improve the efficiency of our CABA™ platform in evaluating additional potential product candidates.



Scientific, Clinical and Commercial Assessment

Through broad literature review and consultation with internal and external experts, we have identified and continue to monitor the universe of diseases where pathogenic B cells are implicated in disease pathophysiology. From this set of possible indications, our team then evaluates each disease based on numerous criteria, which include, but are not limited to:

Biologic Opportunity for Cure

- the presence of the antibody is well established in patients with the clinical manifestations of the disease;
- the identified antibody has been shown to be necessary and sufficient in causing clinical disease;
- there is a correlation between antibody titer and disease activity;
- B cell-depleting therapies or autoantibody reducing therapies are shown or believed to be effective in treating the disease;
- the antibody repertoire has been or can be characterized for the disease;

Identifiable and Underserved Patient Populations

- a routine and established antibody test exists or can be developed for diagnosis and biomarker assessment;
- the clinical course and severity of the disease warrant a cellular therapy despite current standard of care;
- products in development do not have the potential to materially improve outcomes versus the current standard of care;

Evaluation of Preclinical and Clinical Development Pathway

- preclinical *in vitro* and *in vivo* models exist or can be developed; and
- potential clinical trial designs and endpoints appear reasonable and achievable.

In addition to assessing the underlying biologic and clinical rationale for each potential target, we also assess commercial feasibility of CAAR T therapy in various B cell-mediated indications. As part of this assessment, we evaluate the direct lifetime drug and overall healthcare costs due to the burden from the disease, including the costs of managing potential adverse effects from existing standard of care compared to the potential CAAR T therapy.

We perform this rigorous and detailed conceptual analysis to enable us to be thorough and thoughtful before committing significant resources to a program. We believe this analysis allows us to prioritize and advance potential product candidates through the CABA™ platform with a higher degree of confidence and a higher probability of success.

Epitope Mapping

Epitope mapping involves identifying specific sites on the antigen that are responsible for binding to the antibody of interest. This step is required in order to facilitate an understanding of CAAR design and feasibility. An understanding of the locations of the key immunogenic epitopes on the antigen heavily informs the potential feasibility of a CAAR. With an understanding of these epitopes, we then leverage our cell therapy expertise to design the CAAR construct.

CAAR Construct / Design

Our scientists and collaborators design and create multiple CAAR constructs following completion of epitope mapping, which are tested against the antibody or antibodies of interest. The goal in CAAR design is to maximize the inclusion of known immunogenic epitopes on the antigen while also optimizing the size of the construct to improve the ability of the CAAR to bind to the antibody. Determining the location of antigen expression and if there are other antigens that may unintentionally cross-react with the CAAR will also inform CAAR design and feasibility. The size of the antigen will also determine whether a CAAR can be designed based on the size constraints of the delivery system. Once we have designed and developed optimal CAAR constructs, we test them in a variety of *in vitro* and *in vivo* studies.

In Vitro *and* In Vivo *Testing*

In vitro preclinical testing is focused on establishing the specificity and activity of the potential CAAR T cell product candidate against B cells expressing known pathogenic target antibodies. Specificity is evaluated against non-target membrane proteins that may be expressed on other cells, with specific focus against any proteins that are known to bind to the antigen presented on the CAAR. CAAR T function is tested in the presence and absence of soluble, or free, antibodies isolated from patients, since these antibodies may enhance or inhibit CAAR T cell function. Where relevant animal models exist, the CAAR T cell product candidate is tested in one or more models to address specific questions around safety and the ability of the potential product candidate to reduce disease activity *in vivo*.

Pipeline

We are developing a portfolio of CAAR T cell product candidates for the treatment of B cell-mediated autoimmune diseases. Our lead product candidate, DSG3-CAART, targets B cells that express pathogenic autoantibodies against the DSG3 protein, which cause mPV. The publication of the first *in vivo* evaluation of activity and toxicity of the candidate in an animal model was followed by additional preclinical studies to support our IND submission, which was cleared by the FDA in September 2019. The FDA granted our lead product candidate, DSG3-CAART, designed to treat patients with mPV, orphan drug designation for the treatment of PV in January 2020 and fast track designation for improving healing of mucosal blisters in patients with mPV in May 2020. We initiated our DesCAARTes ™ trial in June 2020 and announced the dosing of the first patient in December 2020. In 2021, we announced the 28-day safety data for the first three cohorts in the study along with top-line data on biologic activity from the first two, low dose cohorts in December 2021. In March 2022, we disclosed 28-day safety data for our fourth cohort. Our next PV-directed product candidate, DSG3/1-CAART, targets B cells that give rise to pathogenic autoantibodies against either the DSG3 or DSG1 protein, which cause mcPV, and could address a broader PV population.

Our second product candidate, MuSK-CAART, targets B cells that differentiate into antibody secreting cells that produce pathogenic autoantibodies against the MuSK receptor in patients with MG. In the fourth quarter of 2021, we submitted an IND for the first-in-human studies to the FDA, which became effective in January 2022. In February 2022, MuSK-CAART received fast track designation from the FDA for improving activities of daily living and muscle

strength in patients with MuSK antibody-positive myasthenia gravis. We are also advancing additional product candidates currently in discovery-stage or preclinical development for the treatment of mucocutaneous PV, or mcPV, PLA2R-associated membranous nephropathy, or PLA2R MN, and Hemophilia A with Factor VIII, or FVIII, alloantibodies in addition to two undisclosed targets.

Our Product Candidates

DSG3-CAART for Mucosal PV

Our lead product candidate, DSG3-CAART, is a CAAR T cell therapy expressing DSG3 antigen epitopes as the extracellular domain of a chimeric immunoreceptor, and is designed to enable specific cytotoxicity toward B cells with DSG3 autoantibody targeting abilities. We believe this strategy has the potential to enable direct elimination of DSG3 autoantibody memory B cells and indirect elimination of DSG3-specific short-lived plasma cells that produce the pathogenic autoantibodies.

Scientific, Clinical and Commercial Assessment

PV is a potentially fatal, chronic autoimmune disease characterized by acantholysis, which is the loss of adhesion between cells of the skin or mucous membranes. Desmosomes are a collection of proteins that provide the structure for epithelial cells to connect with each other. PV results when specific pathogenic autoantibodies disrupt desmosomes by targeting DSG3 and/or DSG1, which are proteins that are part of the desmosomes. These autoantibodies cause the upper layer of the epidermis to split away from its base resulting in characteristic erosions and blisters. Widespread damage to the skin and mucous membranes increases susceptibility to life-threatening systemic infections. PV has two major subtypes:

- mPV—Characterized by DSG3 autoantibodies only, affecting only the mucous membranes—accounts for approximately 25% of PV
- mcPV—Characterized by DSG3 autoantibodies and DSG1 autoantibodies, affecting both the mucous membrane and skin—accounts for approximately 75% of PV

The presence of DSG-specific antibodies is 98% to 100% sensitive and specific in identifying patients with PV, and these antibodies have been deemed both necessary and sufficient to cause the disease. Thus, in the absence of DSG autoantibodies, PV generally does not occur. In mPV, patients will typically develop painful skin blisters on their mucous membrane, including mouth, nose, throat, and genitals, often leading to an inability to eat, drink and function normally. The pathogenic DSG3 autoantibody is made by a specific small number of antibody secreting cells, which arise from B cells that express the DSG3 autoantibody on their surface. An overview of mPV and mcPV is provided in the figure below.

	Mucosal PV **25% of U.S. pemphigus vulgaris**	**Mucocutaneous PV** **75% of U.S. pemphigus vulgaris**
		
Associated Antibody	**Anti-DSG3**	**Anti-DSG3 + Anti-DSG1**
Clinical Signs	Painful blisters of the mucous membranes (mouth, nose, larynx, esophagus, eyes, genitalia, rectum)	Blisters on orifices and skin
US Disease Prevalence	**3,250 to 4,750**	**9,750 to 14,250**

Visual evidence of clinical manifestations of PV. (Left panel) Inside of cheek of a patient with mPV, showing sloughing mucosa and blistering. (Right panel) Back of a patient showing cutaneous skin blistering and sloughing in a patient with mcPV. Image credit: D@nderm.

Like most autoimmune diseases, the current standard of care for PV relies on general immune suppression, which is often transiently effective but can lead to severe infection, potentially resulting in hospitalization and death. First-line therapy for PV typically consists of corticosteroids in moderate to high doses in combination with the anti-CD20 monoclonal antibody rituximab where clinically appropriate. Second-line therapy focuses on the several systemically immunosuppressive medications such as mycophenolate, azathioprine, and methotrexate. Additional options used in the acute setting include plasmapheresis, or infusions of intravenous immunoglobulin.

B cell depletion with rituximab was approved by the FDA for the treatment of PV in 2018 and is playing an increasing role as part of the standard of care because it has proven to be one of the more effective therapies for PV. Despite its recent approval for use as a therapy with corticosteroids in PV, rituximab has several limitations in terms of efficacy, safety, and convenience. Rituximab treatment frequently results in relapse, which is reduced but still occurs despite chronic treatment every six months in PV. It does not specifically target the pathogenic B cells, but rather it depletes all CD20-expressing B cells, which leads to an ongoing risk of severe infection and death. As such, there remains not only an unmet medical need in PV, but also a need for safer therapies that can provide a reliable, durable, and complete remission off of all other medications.

There are several emerging therapies also being developed for the treatment of PV, which are being evaluated in late-stage clinical trials. These therapies provide important alternative therapeutic options for patients; however, we believe based on early published data that these therapies are unlikely to be curative and do not specifically ablate autoreactive B cells.

Epitope Mapping

DSG3 consists of five extracellular cadherin, or EC, domains as shown schematically in the figure below. Since T cell activation depends on the intermembrane distance of the immunologic synapse, we tested different combinations of ECs for expression in primary human T cells using DSG3 fragments as the extracellular domain as shown in the figure below.

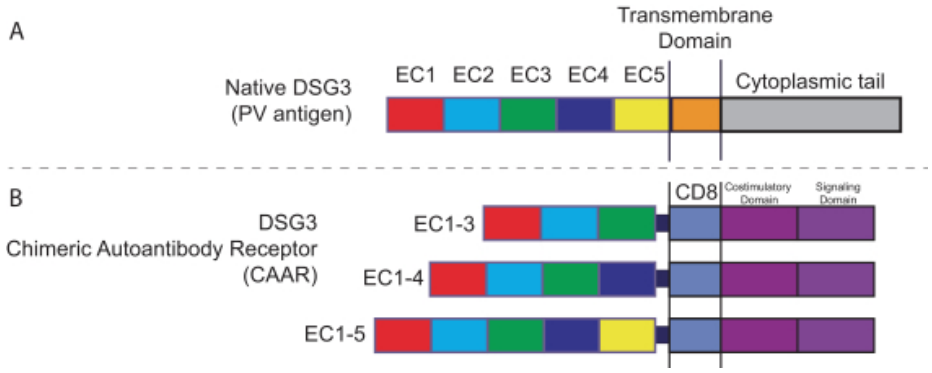
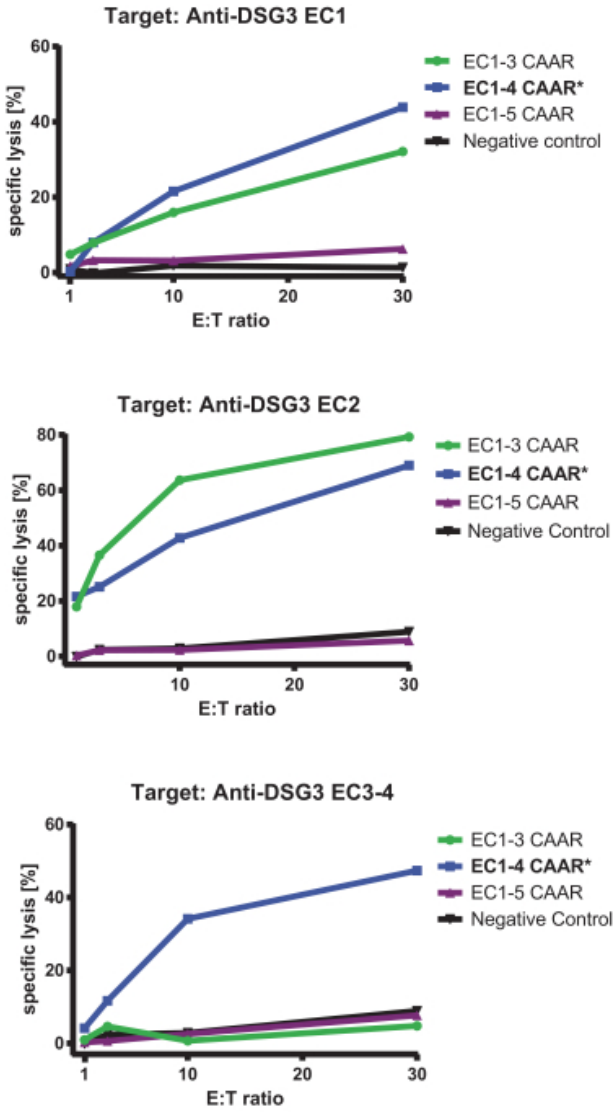


Image showing the naturally occurring DSG3 protein and the five EC domains. (B) The CAAR constructs that were evaluated in preclinical studies, containing the whole or subsets of the DSG3 protein. The transmembrane and intracellular signaling domains are identical to those in the CART19 studies published by Penn.

CAAR Construct / Design

The DSG3 EC1-5 CAAR was minimally functional, likely due to the extracellular domain being too large to enable CAAR function or aggregation of the CAAR on the T cell surface. The CAAR designs with either DSG3 EC1-3 or DSG3 EC1-4 showed interferon-gamma production after exposure to the target cells, demonstrating specific cytotoxic activity across targets. In addition, no cytokine production was detected after exposure to cells that did not express surface immunoglobulins or other non-target cells.

The DSG3 EC1-3 was not effective against one target cell known to bind to the DSG3 EC3-4 domain. Together, this data suggests that the DSG3 EC1-4 CAAR is the optimal construct to balance activity while retaining the ability to target locations of known pathogenic antibodies, as shown in the figures below.



*Cytotoxicity assay to assess killing activity of DSG3 CAART. Negative control is a CAR T with an antibody fragment attached to the extracellular domain. * indicates construct that was selected for further development. E:T ratio = effector to target ratio.*

In Vitro *Studies*

A variety of *in vitro* studies were conducted to evaluate DSG3-CAART from a preclinical activity and toxicity perspective. These studies included an evaluation of DSG3-CAART against proteins that are known to bind the DSG3 antigen, a screen of DSG3-CAART against an array of other membrane proteins and a set of studies designed to evaluate the potential effects of soluble DSG3 antibodies against DSG3-CAART. The results of these studies are summarized below.

Evaluation of DSG3-CAART reactivity against known DSG3 binding proteins. The DSG3 antigen presented on the extracellular domain of DSG3-CAART may naturally bind proteins in the body. These proteins may bind to and activate DSG3-CAART, potentially causing toxicity. The native binding proteins for DSG3 are the desmocollin proteins, which are important for cell adhesion in the skin and mucosa. We performed a variety of studies to test whether DSG3-CAART recognizes and activates the desmocollin proteins. Epithelial cells isolated from various primary organ systems that express some level of desmocollin proteins were screened. Potential DSG3-CAART activity was evaluated through the detection of cytokines released against each cell type and cytotoxicity. The data demonstrated an absence of inflammatory T cell cytokines after being exposed to these cells, indicating an absence of T cell activation. No cytotoxicity was detected except at very high, non-pharmacologically feasible doses. Collectively, we believe there is sufficient evidence to suggest that the DSG3 protein in the context of a CAAR does not meaningfully interact with desmocollin proteins.

Evaluation of DSG3-CAART off-target binding against membrane proteins. A membrane protein array was utilized to screen the DSG3-CAART extracellular domain against 5,300 membrane proteins, which encompass the approximate number of membrane proteins contained in the human genome. The confirmatory screen yielded no off-target signals, except for one weak signal against a protein that is known to bind to glycoproteins, and which was detected in both the test and control conditions. Further evaluation of this protein in cell-based assays indicated that DSG3-CAART does not recognize and activate against this protein.

Evaluation of the effect of soluble antibodies on DSG3-CAART function. We expect that circulating antibodies may prompt an active immune response against treatment with CAAR T cell therapy. These antibodies can induce proliferation of DSG3 CAAR T cells but may also neutralize the cells. In our preclinical *in vitro* studies, we observed that while DSG3 antibodies may have a variable effect on CAAR function, there was no systematic effect to enhance or reduce CAAR function. These dynamics were evaluated in a series of *in vitro* studies as follows:

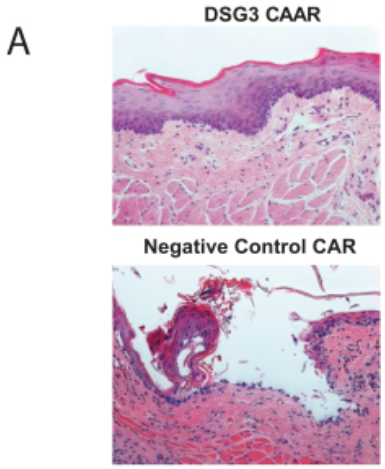
- *Soluble DSG3 antibodies were added to CAAR T cell cytotoxicity assays, at a range of concentrations likely to be encountered in patients, to assess the impact on CAAR function.* In all cases when the CAAR T cells were tested in the presence of soluble DSG3 antibodies, they retained their killing function. In addition, the presence of antibodies did not demonstrate a systematic effect to enhance or reduce the CAAR T cells' cytotoxic ability. Therefore, we believe that removal of circulating soluble DSG3 antibodies from patients prior to infusions may not be necessary to enable potential benefit.
- *Monoclonal DSG3 antibodies with an enhancing effect were evaluated in combination with PV patient serum to assess their impact on DSG3 CAAR T cell division and stimulation of cytokine production.* Monoclonal DSG3 antibodies were capable of inducing DSG3 CAAR T cell division and stimulated production of moderate levels of cytokine production, as measured by interferon gamma. Therefore, we believe the presence of DSG3 autoantibodies in patients may contribute to the DSG3 CAAR T cell population expansion post-infusion.
- *Antibodies purified from PV patients were added to DSG3 CAAR T cells at a range of concentrations known to commonly occur in patients in order to evaluate the extent to which patient serum may activate CAAR T cells.* These antibodies induced a dose dependent increase in interferon gamma.

- *Off-target toxicity may also be seen due to antibody-mediated bridging of DSG3 CAAR T cell cytotoxicity against hematopoietic cells that express receptors designed to bind to antibodies, known as Fc receptors.* To evaluate this, we loaded DSG3 antibodies onto cells expressing antibody-binding receptors, and evaluated the ability of DSG3 CAAR T cells to bind and activate against these targets *in vitro.* No evidence of cytotoxicity was observed, suggesting the potentially low risk of off-target killing mediated by this mechanism.

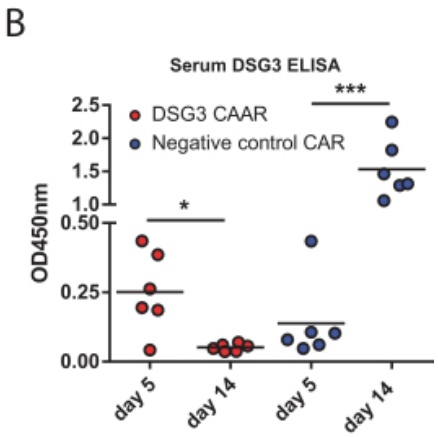
In Vivo *Studies*

To evaluate DSG3-CAART *in vivo*, four murine models were used. These models were designed to directly compare the potency of DSG3-CAART in comparison with CART19 cells; evaluate the potential for on-target skin toxicity; and measure the activity of DSG3-CAART in the presence of polyclonal soluble DSG3 antibodies.

- *Evaluation of potency of DSG3-CAART in a human B cell tumor line compared to CART19 cells.*This B cell model contained genetically-modified B cells to express DSG3 antibodies on the cell surface in addition to luciferase, a bioluminescence marker, and allowed evaluation of DSG3-CAART's ability to engage and kill B cells that express the pathogenic antibody. CART19 cells were used as a positive control in this model as the B cells express CD19 on their cell surface. In this model, DSG3-CAART was found to result in a similar reduction of B cells compared to the CART19 cells.
- *Evaluation of on-target skin toxicity mediated by DSG3-CAART.*A human skin-xenografted model was used to evaluate the potential skin toxicity of DSG3-CAART by evaluating if the extracellular domain would react with desmocollin proteins, which are the known target for DSG3. These results were compared directly to a positive control CAR T expressing a DSG3 specific antibody as an extracellular domain. In this model, we observed the absence of skin toxicity mediated by the DSG3-CAART cells compared to the positive control, which did demonstrate skin toxicity.
- *Evaluation of DSG3-CAART in the presence of soluble antibodies.* We also tested a model where mice have circulating DSG3 antibodies to mimic the situation in PV patients. In this model, the DSG3 antibodies have well-defined and different epitopes with varying affinities, which may reflect the potential breadth of B cell targets that could be encountered in PV patients. The mice were then treated with DSG3-CAART, which was compared to non-CAAR expressing T cells, or negative control CAR T cells. In this model, we observed amelioration of disease (see figure A below), reduction of DSG3 antibody titers (see figure B below), as well as control of the pathogenic B cells (see figure C below), by DSG3-CAART. In this model, DSG3-CAART also demonstrated dose-related activity, particularly in regard to reduction of serum autoantibodies, epithelial-bound autoantibodies (not shown in Figures) and DSG3-CAART engraftment, suggesting that higher DSG3-CAART doses may promote engraftment (see Figures D and E). We believe these results show the functional activity of DSG3-CAART in the presence of soluble antibody.

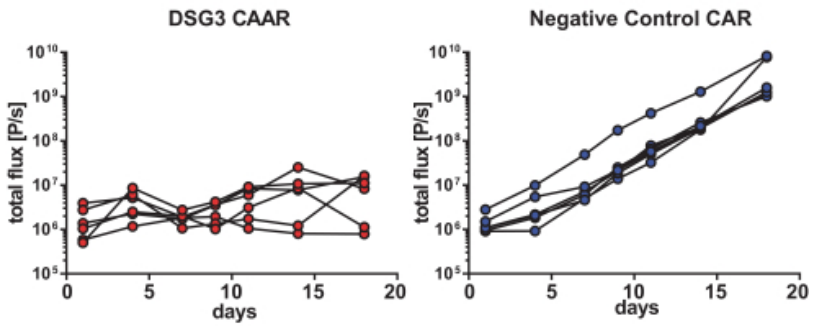


Histology showing DSG3 CAAR maintaining normal epithelial cell structure in treated animals.



*OD450 is a proxy measure for anti-serum DSG3antibodies in the blood. * indicates statistically significant reduction in DSG3 serum antibody level in DSG3-CAART treated mice. P value is < 0.05. *** indicates statistically significant increase in DSG3 serum antibody level in the negative control CAR treated group. P value is < 0.001.*

C



Total flux is a quantitative measure of cell bioluminescence, which approximates cell activity in this assay.

D

*OD450 is a proxy measure for the level serum anti-DSG3 antibodies in the blood. Serum anti-DSG3 ELISA was performed on day 10 for all mice with remaining serum samples available, indicating that mice treated with the 3x10^7 and 1x10^7 DSG3-CAART dose effectively reduced serum anti-DSG3 IgG production compared to mice treated with NTD T-cells or the 3x10^6 DSG3-CAART dose.** indicates statistically significant reduction in DSG3 serum antibody level in DSG3-CAART treated mice. P value is < 0.01. * indicates statistically significant increase in DSG3 serum antibody level in the negative control CAR treated group. P value is < 0.05. ns indicates a non-significant difference.*

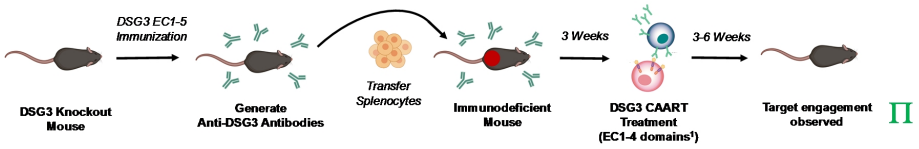
E

Quantification by flow cytometry of CD3-positive T-cells in peripheral blood on day 10 and 17 is shown. The data support dose-related DSG3-CAART engraftment based on increased CD3+ cells with increased DSG3-CAART dose.

- *Evaluation of DSG3-CAART in an active immune model.* An exploratory active immune mouse model for PV was developed to better represent the human phenotype in autoimmune disease. This model involved generating anti-DSG3 B cells in a mouse without DSG3 by repeated immunization with human DSG3. Splenocytes containing anti-DSG3 B cells from the immunized mouse were transferred into an immunodeficient mouse to generate the PV phenotype. These mice produced DSG3 antibodies against multiple extracellular domains of the DSG3 antigen, including EC5, at physiologic levels comparable to those observed in PV patients. Treatment with DSG3 EC1-4 CAAR T cells, in the absence of preconditioning, effectively lowered serum DSG3 antibody levels by ELISA, reduced antibodies against relevant DSG3 domains by epitope mapping and reduced blistering by histology. These mice retained autoantibodies targeting the DSG3 EC5 region, though the mice did not show clinical manifestations of PV.

- See figure F below for a schematic representation of the experiment.

F



Schematic representation of the PV active immune model. A DSG3 knockout mouse is immunized with DSG3 EC1-5. The knockout mouse develops antibodies against DSG3 across all EC domains. The splenocytes from the knockout mouse are transferred to an immunodeficient mouse where the DSG3 antibodies cause a clinical phenotype consistent with PV. Those mice are then treated with DSG3-CAART (EC1-4 domains only).

Clinical Development Plan

The FDA cleared our IND for a Phase 1 trial of DSG3-CAART in September 2019. The FDA granted DSG3-CAART orphan drug designation for the treatment of PV in January 2020 and fast track designation for improving healing of mucosal blisters in patients with mPV in May 2020. We announced that the first patient was dosed in the DesCAARTes™ trial in December 2020, and enrollment is currently ongoing.

The DesCAARTes™ trial is an open-label trial to assess the safety and tolerability of various dosing regimens of DSG3-CAART in the treatment of subjects with active mPV. DSG3-CAART is administered by intravenous infusion, using a fractionated-dose infusion scheme of escalating numbers of DSG3-CAART cells for the initial cohorts in the first phase. This dosing scheme was designed to reduce the potential risks associated with acute infusion-

related toxicities while preserving potential benefit for subjects by allowing a total infused dose that we believe is large enough to be potentially therapeutic based on prior CAR T trials.

We expect that the Phase 1 trial will have three parts:

- Part A: Fractionated dose escalation
- Part B: Fractionation reduction at the selected dose
- Part C: Expansion phase at the selected dose and administration scheme

In Part A, the split dose uses dose fractionation to accommodate a low number of cells in the first infusion while still advancing the dose within the cohort up towards and spanning the range of cell doses that have been therapeutic in past gene-engineered T cell therapy trials. In Part B, the dose selected from Part A will be delivered in a decreased number of dose fractionations to determine the dose fractionation strategy. In Part C, subjects will be enrolled at the dose and fractionation, as determined in Part A and B, to generate additional safety and outcome data to support the rationale for and design of future clinical trials.

Patients are eligible to be enrolled if they have a confirmed diagnosis of mPV based on biopsy for histology and positive DSG3 ELISA; active disease at screening; elevated DSG3 by ELISA at screening; and previously been inadequately managed by, or refractory to, or relapsed after, or with contraindications to or intolerance of at least one prior systemic therapy. The primary objective of the trial is to evaluate the safety of DSG3-CAART cells, and secondary objectives include evaluating the initial signs of target engagement.

We believe the risk of cytokine release syndrome, or CRS, a potentially life-threatening toxicity that has been observed after treatment with some types of immunotherapy, may be reduced with our CAAR T cells, due to its correlation with target cell burdens. In the context of treating cancer, the target cell population consists of all B cells (healthy and cancerous), whereas our CAAR T cells only target the small subset of disease-causing reactive B cell population. While the possibility of cytokine release in a clinical trial resulting from strongly activating soluble antibody cannot be ruled out, to date we have not observed any evidence of it in preclinical studies.

The primary endpoint of the study is the incidence of adverse events within three months of DSG3-CAART infusion, including dose limiting toxicity defined as occurring within 28 days of infusion. The FDA has requested, and we have agreed, that we will share data from cohort A to inform a discussion on the optimal design of cohort C. According to FDA guidance, the submission of cohort A data is not gating to planned enrollment in cohort B and the FDA plans to provide feedback, if any, in a timely manner.

In May 2021, we reported the acute safety data from the first cohort of patients in the DesCAARTes™ trial, where no DLTs had been observed eight days after infusion in the first three patients who received DSG3-CAART. DSG3-CAART was detected at low levels in both patients who had been evaluated and completed the DLT period at that time. In August 2021, with FDA clearance, a protocol amendment was implemented in the DesCAARTes ™ trial to allow a minimum dosing interval of seven days between patients within a cohort, versus 14 days. In August 2021, we also reported the 28-day safety data from the second cohort of patients in the DesCAARTes ™ trial, where no DLTs had been observed 28 days after infusion in the second cohort of three patients who received DSG3-CAART. DSG3-CAART persistence was observed via quantitative polymerase chain reaction in peripheral blood samples of all three patients in the second dose cohort during the 28 days following infusion. In November 2021, we reported that dose dependent increases in DSG3-CAART persistence in the third cohort relative to the first two low dose cohorts throughout the 28 days following infusion have been observed, as well as the continued absence of any DLTs or clinically relevant adverse events for the first three cohorts.

In December 2021, we reported biologic activity data from the six patients in the two lowest dose cohorts in the DesCAARTes™ trial with three to six months of follow-up evaluation. Parameters being used in the trial to evaluate potential biologic activity include persistence of DSG3-CAART, change in level of DSG3 autoantibodies, change in mPV therapy or need for new systemic rescue therapy, and change in disease activity (e.g., assessed by Pemphigus Disease Area Index, or PDAI, and Oral Disease Severity Score, or ODSS). Top-line data on biologic activity among the first six participants in the lowest dose cohorts demonstrated no clear indications of biologic activity at doses that represent less than 2% of the current planned maximum dose in the trial. In the cohort receiving the 20 million DSG3-

CAART cell dose, two patients worsened, and one patient improved. As permitted by protocol, the patient that improved was enrolled due to worsening symptoms despite receiving two different systemic therapies within nine months of DSG3-CAART infusion. The systemic therapies may have impacted clinical scores and DSG3 levels, both of which improved between screening and infusion. In the 100 million dose cohort, one patient had stable disease, one patient was stable then had increasing disease activity, and one patient worsened. Furthermore, we announced the continued absence of any DLTs or clinically relevant adverse events.

As reported in November 2021, a dose-dependent increase in DSG3-CAART persistence in the 500 million cell dose cohort was observed relative to the two lowest dose cohorts throughout 28 days post-infusion, and patients in the fourth cohort are receiving 2.5 billion DSG3-CAART cells, which is 25 and 125-fold greater than the two dose cohorts reported at the end of 2021.

In the December 2021 announcement, we also reported that, based on the safety profile observed to date and FDA communications dating to early 2021, additional cohorts are planned to evaluate increased doses, consolidated fractions, and, subject to a protocol amendment, an enhanced manufacturing process which aims to amplify the already present cell subtypes in the product in order to potentially improve product potency and trafficking to tissue where the target B cells reside. The additional fifth cohort will receive between 5.0-7.5 billion DSG3-CAART cells with a more consolidated fractionated infusion dosing regimen including only two fractions.

In January 2022, we announced that 28-day safety data for the fourth cohort was anticipated to be announced in the first quarter of 2022, and that other clinical data updates from the DesCAARTes™ trial are expected to be provided at scientific meetings throughout 2022 and 2023 with biologic activity data for cohorts A3 and A4 expected to be announced in mid-2022. In February 2022, FDA cleared our protocol amendment regarding the planned enhanced manufacturing process. In March 2022, we disclosed 28-day safety data from the fourth cohort of patients in the DesCAARTes™ trial, where no DLTs had been observed 28 days after infusion in the three patients who received DSG3-CAART at the 2.5 billion cell dose level. In addition, we disclosed that we are currently enrolling patients for the fifth cohort, and expect to announce 28-day safety data for the fifth cohort at a scientific meeting in mid-2022, assuming no DLTs are observed during such cohort, that enrollment is uninterrupted and no there are no delays due to COVID-19 resurgence. We also currently intend to announce serious adverse events, if any, if they materially change timelines or the trial design.

DSG3/1-CAART for mcPV

Scientific and Commercial Assessment

Our next PV product candidate, DSG3/1-CAART, is being designed to target DSG3 and/or DSG1 autoantibodies on pathogenic B cells that cause mcPV. mcPV is the most severe and most common subtype of PV and affects approximately 75% of PV patients. While mPV is caused by DSG3 autoantibodies, mcPV involves autoantibodies to both DSG3 and DSG1, resulting in the additional involvement of skin erosion and blistering. Similar to mPV, mcPV is typically treated with immune suppression, which has a high rate of relapse and potential for hospitalizations and fatal infections.

Epitope Mapping

DSG1 consists of five EC domains, with all known pathogenic epitopes occurring in the DSG1 EC1-4 domains. Similar to development of DSG3-CAART, we tested different combinations of DSG1 ECs for expression in primary human T cells using DSG1 fragments as the DSG1 EC domains. Given prior development of DSG3 CAAR, we leveraged those findings in the design of our DSG1 CAAR.

CAAR Construct / Design

We also tested multiple combinations of EC domains of DSG1 CAAR administered alone and in combination with the DSG3 EC1-4 CAAR to evaluate for cell-surface expression of the CAAR along with the potency and breadth of target cell killing. In this setting, the DSG1 EC1-4 CAAR showed robust and specific cytotoxicity towards all known pathogenic epitopes.

In Vitro *Studies*

CAAR development for mcPV, based on the targeting of DSG3- and/or DSG1-specific B cells, has shown promising preclinical results. DSG1 CAAR T cells specifically killed DSG1-specific B cells *in vitro*. In addition, we observed that with a 1:1 mixture of DSG3 and DSG1 CAAR T cells had killing capabilities without synergistic or antagonistic effect.

In Vivo *Studies*

The activity and toxicity of DSG3 and DSG1-CAAR T cells was evaluated using human skin xenografts in comparison with anti-CART19 cells, which are known from human clinical trials not to cause direct skin toxicity. A 1:1 mixture of DSG3 and DSG1 CAAR T cells did not show off-target toxicity *in vivo.*

Development Plan

From a regulatory and clinical trial design perspective, we anticipate that many of the elements incorporated into the planned DesCAARTes™ trial will carry over to DSG3/1-CAART. We plan to evaluate the initial cohorts of patients from the planned DesCAARTes ™ trial for safety and evidence of target engagement prior to proceeding with an IND submission for DSG3/1-CAART. We believe that, because mcPV is the most prevalent subset of PV and the patients are generally followed by the same subspecialists, it will allow for a wider patient pool eligible for a clinical trial. We anticipate the DSG3/1-CAART clinical trial design will have a significant amount of overlap with the DSG3-CAART trial design, but it will be informed by clinical data from the early cohorts in the DesCAARTes™ trial. We further anticipate being able to use the same centers from the DesCAARTes™ trial to enroll patients for the DSG3/1-CAART clinical trials.

We are currently evaluating advanced manufacturing technologies that would potentially allow us to administer DSG3/1-CAART as a single product rather than requiring separate administration. The size of the DSG3/1 product candidate will likely require us to incorporate additional technologies to accommodate the size of the final CAAR construct. An evaluation of potential technologies to achieve this objective is ongoing. Upon completing the evaluation of these manufacturing technologies, we expect to conduct additional *in vitro* and *in vivo* studies using the combined product. While a product that administers a DSG3 CAAR and DSG1 CAAR as two separate products may be feasible, we believe that there would be significant advantages to developing a combined product from a regulatory and commercial perspective.

MuSK-CAART for MuSK Myasthenia Gravis

Scientific, Clinical and Commercial Assessment

MG is an autoimmune disease induced by autoantibodies targeting the neuromuscular junction, or NMJ, which can lead to life-threatening muscle weakness. Generalized MG, or gMG, is characterized by profound muscle weakness throughout the body, which may result in motor impairment, disabling fatigue, shortness of breath due to respiratory muscle weakness and episodes of respiratory failure.

gMG affects approximately 50,000 to 80,000 patients in the United States. The majority of patients who develop gMG have autoantibodies against some part of the NMJ that are known to be pathogenic. 80% to 90% of patients with gMG have autoantibodies against the acetylcholine receptor, or AChR, detectable in their serum. Approximately 6% to 7.5% of patients with gMG have autoantibodies against MuSK, which is a different target on the surface of the muscle membrane.

Patients diagnosed with MuSK MG have a different recommended treatment course compared to patients withAChR MG. Importantly, many patients with MuSK MG respond poorly to cholinesterase inhibitors, which are often the first line of therapy in AChR MG. Consequently, patients with MuSK MG are typically started on corticosteroids in addition to one or more steroid-sparing immunosuppressive agents. Corticosteroids are tapered to the extent possible to prevent disease relapse, though many remain dependent on corticosteroid despite concomitant treatment with immunosuppressive medications. In the acute setting, plasma exchange or intravenous immunoglobulin may be used to address severe disease. Rituximab is often considered as a second-line therapeutic option in patients with an inadequate response to initial immunosuppressive medications. Importantly, complement is not thought to be meaningfully implicated in the pathophysiology of MuSK MG, and complement inhibitors are not indicated for treatment of disease.

Epitope Mapping

The MuSK protein has a similar structure and size as compared to DSG3. MuSK contains four extracellular domains, as shown below.

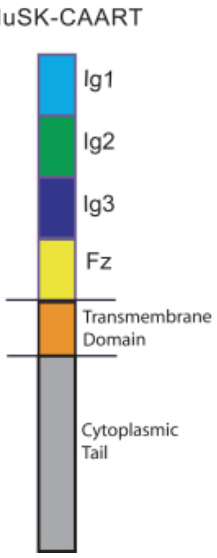


Figure illustrating the domains of the wild-type MuSK protein.

Studies conducted in patients with MuSK MG have revealed that the autoantibodies may be against epitopes located in each of the extracellular domains for MuSK.

CAAR Construct and Design

With an understanding that pathogenic autoantibody epitopes may target any domain of MuSK, multiple MuSK CAAR candidates have been engineered that incorporate all extracellular domains. Each CAAR construct is being or will be tested in preliminary *in vitro* and *in vivo* experiments.

In Vitro *Studies,* In Vivo *Studies and Development Plan*

Data from our initial *in vitro* and *in vivo* studies of MuSK-CAART was presented at the American Academy of Neurology's Science Highlights Virtual Platform in May 2020. The efficacy and safety of MuSK CAAR T cells were investigated using *in vitro* cytotoxicity assays, *in vitro* screens for off-target toxicity and a mouse model to evaluate the efficacy of human MuSK CAAR T cells against MuSK antibody expressing B cells *in vivo*. In preclinical studies, MuSK CAAR T cells containing the native MuSK extracellular domain demonstrated *in vitro* cytotoxicity towards a panel of B cells expressing anti-MuSK antibodies specific for different extracellular regions of the MuSK protein, but no observed cytotoxicity when anti-MuSK antibodies are not expressed (figure below). Additionally, MuSK CAAR T cells did not demonstrate cytotoxicity toward cells expressing LRP4, which is a different protein in the neuromuscular junction that can bind with naturally occurring MuSK in certain configurations.

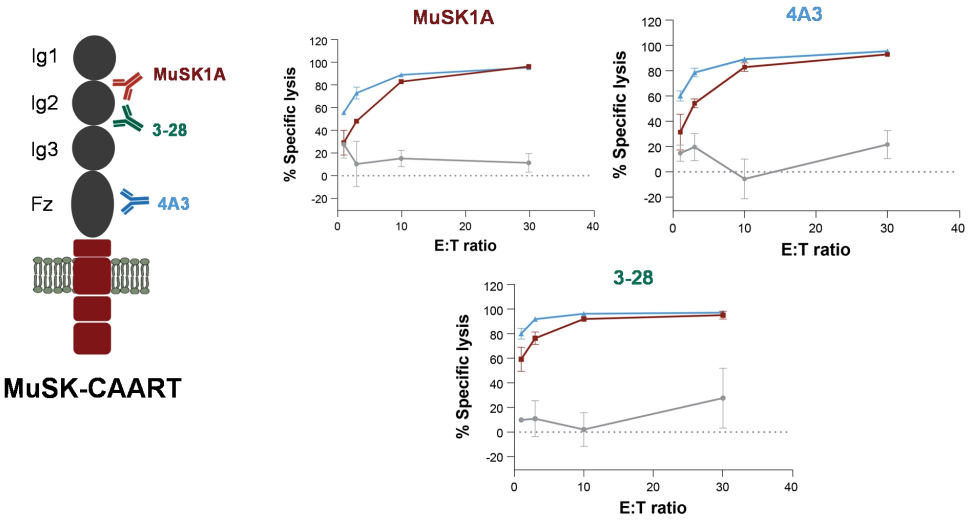


Figure illustrating that MuSK-CAART, which contains the native MuSK extracellular domain, demonstrated selective and specific in vitro cytotoxicity towards a B cell line expressing anti-MuSK antibodies targeting different MuSK epitopes across multiple domains of the native MuSK protein. The specific lysis increases directly with increasing effector to target ratios for MuSK-CAART.

As illustrated in the figure below, in an *in vivo* mouse model, MuSK CAAR T cells, but not control CAAR T cells, showed biological activity by blocking the growth of B cell lines expressing an anti-MuSK antibody.

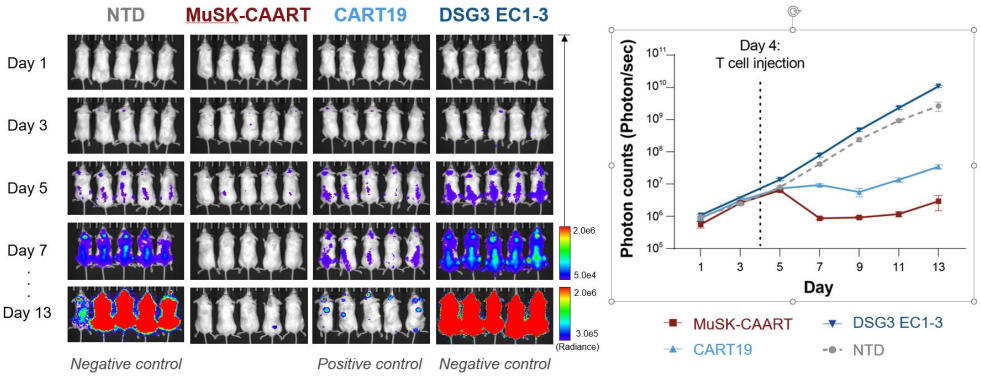


Figure illustrating MuSK CAAR T cells are able to recognize and suppress anti-MuSK target cells in a murine model. The target cells express both CD19 and anti-MuSK B cell receptors, and CART19 is used as a positive control in this experimental system.

Clinical Development Plan

Based in part on these preclinical results, IND-enabling studies were completed for the MuSK-CAART product candidate. In the fourth quarter of 2021, we submitted an IND to the FDA for MuSK-CAART, which became effective in January 2022. In February 2022, MuSK-CAART received fast track designation from the FDA for improving activities of daily living and muscle strength in patients with MuSK antibody-positive myasthenia gravis. We plan to initiate the MusCAARTesTM trial in 2022.

The MusCAARTesTM trial is an open-label trial to assess the safety and tolerability of various dosing regimens of MuSK-CAART in the treatment of subjects with active MuSK MG. MuSK-CAART is administered by intravenous infusion, using a single infusion of MuSK-CAART cells at a starting dose informed by initial clinical data from the DesCAARTesTM trial and prior CAR T trials.

We expect the Phase 1 trial will have two parts:

- Part A: Dose escalation
- Part B: Expansion phase at the selected dose

In Part A, the dose will initially begin at 100 million MuSK-CAART cells, and plans to escalate up to 7.5 billion MuSK-CAART cells in four dose cohorts. Cohort A2 is planned at 500 million MuSK-CAART cells, cohort A3 is planned at 2.5 billion MuSK-CAART cells and cohort A4 is planned at 5.0 to 7.5 billion MuSK-CAART cells. We plan to enroll approximately 12 subjects in Part A, subject to observation of DLTs, with at least two patients planned per cohort and a total of 6 subjects to be dosed at the selected dose for Part A. In Part B, subjects will be enrolled at the dose determined in Part A to generate additional safety and outcome data to support the rationale for and design of future clinical trials. We plan to enroll approximately 12 subjects in Part B.

Patients are eligible to be enrolled if they have a confirmed diagnosis of MuSK MG based on a positive anti-MuSK antibody test; myasthenia gravis severity Class I-IVa, a Myasthenia Gravis Composite Score ≥4 and a history of a negative anti-AChR antibody test. The primary objective of the trial is to evaluate the safety of MuSK-CAART cells, and a key secondary objective is to evaluate the initial signs of biologic activity. The primary endpoint of the study is the incidence of adverse events within three months of MuSK-CAART infusion, including dose limiting toxicity defined as occurring within 28 days of infusion.

PLA2R-CAART for PLA2R MN

Scientific and Commercial Assessment

Primary MN is an immune-mediated kidney disease caused by autoantibodies against phospholipase A2 receptor (PLA2R), a single-pass transmembrane protein expressed in the glomerulus of the kidney. Since the discovery of anti-PLA2R autoantibodies in 2009, evidence has shown that these autoantibodies accumulate as immune complexes in the glomeruli of the kidney and damage the filtration barrier, leading to nephrotic syndrome as characterized by proteinuria. Many patients with PLA2R-associated MN are at risk for progression to kidney failure.

Primary MN affects approximately 15,000 patients in the United States and is associated with autoantibodies directed to PLA2R in 70-80% of patients. Immunosuppressive treatments are commonly used to treat MN, with increasing use of B cell-depleting therapies such as rituximab in the first line for medium to high-risk patients. However, high unmet need remains, as a significant fraction of patients either relapse or fail to respond following treatment with immunosuppressive therapies. By selectively depleting the PLA2R autoantibody expressing B cells that cause disease, we believe PLA2R-CAART could provide a potentially safe, effective, and durable therapeutic option for patients with PLA2R-associated MN.

Epitope Mapping

PLA2R is a single-pass transmembrane protein with distinct immunogenic regions. The protein consists of a cysteine rich domain, a fibronectin type II domain, and eight C-type lectin domains, as depicted below.

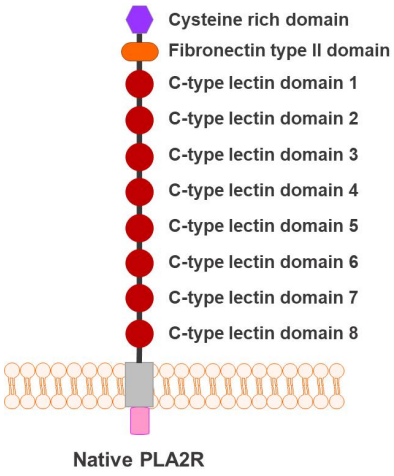


Figure illustrating the domains of the wild-type PLA2R protein.

Studies have demonstrated that the cysteine rich domain is the immunodominant epitope in PLA2R MN, and autoantibody reactivity to C-type lectin domains one and seven portend a worse prognosis.

CAAR Construct / Design

Based on the well-defined epitopes of PLA2R, multiple PLA2R CAARs have been designed to incorporate key antigenic regions and to evaluate epitope conformation. The engineering of preliminary PLA2R CAAR constructs is being led by Dr. Payne, one of our scientific co-founders.

In Vitro *Studies*

As presented at the American Society of Nephrology Kidney Week in the fourth quarter of 2021,*in vitro* cytotoxicity and patient IgG adsorption assays have established the preliminary activity of PLA2R-CAART cells for antigen-specific B cell depletion in PLA2R MN. Multiple PLA2R-CAART cells caused specific lysis of anti-PLA2R hybridomas, and PLA2R CAARS adsorbed the majority (>95%) of anti-PLA2R IgG autoantibodies in MN sera. As depicted below, PLA2R-CAART cytotoxicity was preserved over time with physiologic levels of PLA2R MN plasma IgG. Though PLA2R MN IgG inhibited PLA2R-CAART cytotoxicity initially, the cytotoxicity increased with time, likely due to CAART cell proliferation and/or new CAAR synthesis.

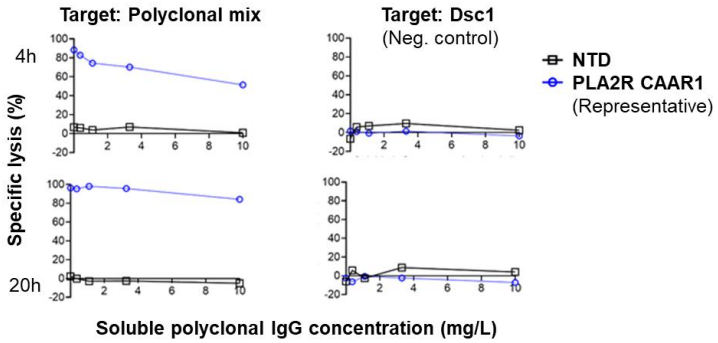


Figure illustrating PLA2R-CAART cells were able to maintain cytotoxicity against anti-PLA2R hybridomas in the presence of physiologic concentrations of PLA2R MN plasma IgG. Though PLA2R MN IgG had some short-term inhibition of PLA2R-CAART cells, cytotoxicity increased with time, likely due to CAART cell proliferation and/or new CAAR synthesis. Cells expressing desmocollin-1 were used as a negative control.

To evaluate for preclinical signals of safety, high throughput screening for off-target PLA2R CAAR interactions was performed, and no off-target binding interactions were identified.

Development Plan

We anticipate that many of the learnings from our more advanced CAART programs will provide expertise in developing a clinical and regulatory strategy for PLA2R-CAART, and we plan to employ therapeutic area-specific strategies, such as the fact that PLA2R antibody levels correlate with proteinuria, a commonly used surrogate endpoint in clinical trials. We conducted a pre-IND interaction with the FDA to discuss the development path for PLA2R-CAART in the fourth quarter of 2021.

FVIII-CAART for Hemophilia A with Factor VIII Alloantibodies

While our CABA™ platform is primarily directed towards the treatment of B cell-mediated autoimmune diseases, we believe the approach may be applicable in other instances where B cell antibody production is implicated. Specifically, we have identified an opportunity to apply the CABA™ platform to develop potential CAAR adjunctive therapies in cases where the immune system has or produces antibodies against potential therapies, which is known as an alloimmune response. These alloantibodies can prevent a particular therapy from being delivered effectively because the therapy is degraded by the immune response due to alloantibody binding. We believe our approach has the potential to address the alloantibody response by specifically ablating the B cells responsible for producing the alloantibodies through a similar mechanism seen in autoimmune disease. With the alloantibody producing cells ablated, the treatment could then be provided.

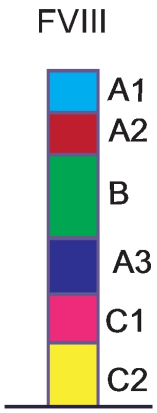
Scientific, Clinical and Commercial Assessment

Hemophilia A is an X-linked bleeding disorder caused by mutations in the FVIII gene resulting in a deficiency of functional FVIII, a critical factor in blood coagulation. It affects about 1:5,000 male births. Severe Hemophilia A, where FVIII levels are less than 1% of normal, accounts for about 60% of all cases and is characterized by frequent spontaneous bleeds. Currently, Hemophilia A is treated with FVIII replacement via intravenous administration.

The main complication of FVIII replacement therapy is that 20% to 30% of patients with severe disease develop neutralizing alloantibodies against the FVIII protein. These alloantibodies decrease the levels of FVIII and at high titers, render attempts to replace or stimulate the production of FVIII ineffective. The risk of alloantibody development for patients with severe Hemophilia A is highest during their initial FVIII exposures. The standard treatment to reverse alloantibody formation consists of repeated high-dose infusions of FVIII, which has limited efficacy, a high cost and is difficult to titrate to an appropriate therapeutic level for the patient. We believe FVIII-CAART could be effective in addressing patients with Hemophilia A who have developed FVIII antibodies that require repeated, high-dose administrations of FVIII.

Epitope Mapping

The following image depicts FVIII, which is a large glycoprotein consisting of six domains that interact with each other to form the full complex.



Studies conducted in patients with Hemophilia A have revealed that acquired FVIII alloantibodies following exogenous FVIII administration are typically directed against A2, C1 and C2 domains of FVIII.

CAAR Construct and Design

Preliminary FVIII CAAR and CAAR-like constructs have been engineered that target key parts, but not all, of the FVIII domains. Dr. Milone, one of our scientific co-founders, has led the development of multiple constructs to evaluate the impact on safety and potency.

Development Plan

We are conducting additional studies to optimize our FVIII-CAART development. The focus of these ongoing studies is to fully characterize the safety and potency of candidate constructs *in vitro* and *in vivo*. Given the size of the FVIII protein, this may require us to utilize alternate gene transfer technology to accommodate the size of the final CAAR construct. Proof of concept studies targeting this objective are ongoing.

Manufacturing

Manufacturing Strategy

We intend to implement a three-stage plan that we believe will ultimately enable us to achieve manufacturing independence. Part of our strategy relies on engaging non-profit and commercial suppliers early and in a staged manner. We believe partnering with proven and reputable manufacturing partners will allow us to efficiently deploy financial and personnel resources. Stage 1 of this plan is in place and utilizes the deep expertise in cell and vector manufacturing from our partners at Children's Hospital of Philadelphia, or CHOP, and Penn. This included early development work, support of the DSG3-CAART IND, and cell and vector product manufacturing for our DesCAARTes™ trial. We believe these facilities will allow us to move efficiently into clinical trials but are not sufficient to support a commercial license.

Stage 2 of our plan is designed to engage partners who are qualified for manufacturing of vector at commercial grade and scale and cell therapy products. We are aware that changes in any manufacturing process or facility introduces regulatory and scientific risk to a development program, if the changes result in a product that is not comparable. We plan to mitigate these risks primarily in two ways:

1. *By securing contract manufacturing organizations, or CMOs, as partners during Stage 2 of our manufacturing strategy early on for both vector and cell manufacturing.* We plan to prioritize potential partners who are qualified to, and have an established track record of, the commercial production of vector and cell products. We believe this allows us to make one change in our supply partners during an early period of clinical development to facilitate *in vitro* comparability testing and clinical validation, prior to controlled clinical studies. As part of this strategy, in January 2021, we initiated a collaboration with WuXi to serve as our cell processing manufacturing partner for our planned MusCAARTes ™ trial. Engineering runs confirming successful technology transfer of our manufacturing process have been completed in preparation for the planned MusCAARTes ™ trial initiation in 2022. In December 2021, we entered into a license and supply agreement with Oxford Biomedica to supply lentiviral vector for the clinical and commercial development of our DSG3-CAART candidate.
2. *By licensing the cell manufacturing process used for our planned Phase 1 DSG3-CAART first-in-human study from Penn.* This is allowing us the time to understand the process used in order to reduce the chance of changes that may impact comparability.

In addition to Stage 2, and contingent on sufficient clinical evidence from our planned DesCAARTes™ trial, we are further planning to pursue Stage 3 in manufacturing supply. During Stage 3, we plan to lease, build, qualify and run our own manufacturing facility. We believe this additional stage will enable full control of continuous improvement, product development and commercial supply for products arising from our CABA™ platform. Our Chief Executive Officer and our President, Science and Technology have both, in prior roles, built and led organizations that have constructed and commissioned cell therapy facilities.

Vector Manufacturing

The lentiviral vector that we plan to use in the initial subjects in our DesCAARTes™ trial was manufactured at CHOP. We have also reserved multiple vector manufacturing slots at Penn and CHOP, which we may use in our DSG3-CAART or subsequent clinical trials. In parallel, we have engaged in development work with multiple CMOs to secure production slots for vector which may be used in our DSG3-CAART or subsequent clinical trials. In December 2021, we entered into a license and supply agreement with Oxford Biomedica to supply lentiviral vector for the clinical and commercial development of our DSG3-CAART candidate. We believe these efforts will provide us with sufficient clinical-grade vector to move forward with our anticipated clinical trials.

Cell Manufacturing

We have entered into a collaboration with the Clinical Cell and Vaccine Production Facility, or CVPF, at Penn, to provide focused scientific, technical and regulatory support for CAAR T cell manufacture. CVPF is accredited by the Foundation for the Accreditation of Cellular Therapy and is capable of and experienced at supporting manufacture for early-phase clinical trials of novel cell therapy products in first-in-man clinical trials. We expect to rely upon CVPF to provide initial Phase 1 clinical trial drug supply for DSG3-CAART. Penn's manufacturing process for DSG3-

CAART is directly related to the process developed at Penn for early clinical trials of CART19, which subsequently became known commercially as Kymriah. The process was later transferred to Novartis Pharmaceuticals Corporation and further modified for the Kymriah program.

As we scale our manufacturing of DSG3-CAART and our other product candidates to meet our expected needs for further clinical trials, we may or may not rely on Penn, but we also expect to rely on CMOs and other third parties for the manufacturing and processing of our clinical trial materials. Any CMO that we select will be subject to cGMP requirements. We believe the use of contract manufacturing for our pipeline programs will be cost-effective and allow us to rapidly prepare for clinical trials in accordance with our development plans. In preparation for this transition, we have engaged multiple third-party contractors to manufacture clinical grade viral vector used to deliver the applicable CAAR gene into the T cells. We have also initiated development work with certain contractors for cGMP and commercial vector production. We expect third-party manufacturers will be capable of providing and processing sufficient quantities of our product candidates to meet anticipated clinical trial demands and commercial need. In January 2021, we initiated a collaboration with WuXi to serve as our cell processing manufacturing partner for our planned MusCAARTes™ trial.

Once we have sufficient clinical data from subjects in our DSG3-CAART study, we intend to begin the process of engineering and then establishing our own commercial scale GMP-compliant manufacturing facility. We believe this will allow us to enhance supply chain control, increase supply capacity and help ensure clinical and commercial demand for our pipeline programs is met in the event that DSG3-CAART receives marketing approval. Informed by our experience in building cell therapy facilities and creating supply chains, we plan to develop a robust supply chain with alternative sources to maintain continuous supply. In parallel with these activities, we are evaluating and executing proof-of-concept studies to test advanced manufacturing and automation technologies to continuously improve the manufacturing process and meet commercial and scalability targets.

Commercialization

Our aim is to become a fully integrated cellular therapy company in order to improve the lives of patients with B cell-mediated autoimmune diseases. We have designed a strategic approach to move forward with our lead product candidate, DSG3-CAART, while at the same time having a number of product candidates in development. The product candidates from our CABA™ platform address clinical indications where there is a compelling opportunity to improve clinical outcomes in comparison with the current standard of care in an easily identified patient population. Our initial product candidates are focused on rare disease populations where we believe there is potential to commercialize independently. This is due to a concentration of treatment paradigms and limited but easily identified patient populations. Our plan is to focus commercialization and launch efforts initially in the United States, and eventually in the European Union and Asia-Pacific geographies.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong focus on intellectual property. We face competition from many different players, including large and specialty pharmaceutical and biotechnology companies, academic research organizations and governmental agencies. Any therapeutic candidates we successfully develop and commercialize will compete with the existing standard of care as well as any novel therapies that may gain regulatory approval in the future.

Existing treatment options for PV are limited. Rituximab, marketed by Roche Holding AG, is the first drug to have received approval for PV in the United States in over 60 years. In Europe, the approved therapies for PV are corticosteroids, azathioprine, and rituximab. Other standard of care treatments include various immunosuppressants, plasmapheresis, and intravenous immunoglobulin infusions given monthly or on another periodic chronic basis. Additionally, multiple biopharmaceutical companies have therapies in clinical development.

Competition in the MuSK MG autoimmune space is currently dominated by the current standard of care, rituximab. A second approved approach to treating patients is IVIG, which is available through CSL Behring LLC, Grifols, S.A., and Mitsubishi Tanabe Pharma Corporation. Additionally, multiple biopharmaceutical companies have therapies in clinical development.

Multiple therapies are approved or in development for the treatment of Hemophilia A patients who develop alloantibodies against FVIII. Standard of care is typically immune tolerance induction, or ITI, therapy with higher doses of FVIII. Available treatments for those who do not respond to ITI include anti-inhibitor coagulation complexes, recombinant factor VIIa, and bispecific factor IXa- and factor X-directed antibodies. Companies who market products or are developing product candidates within these categories of medicine include Catalyst Pharmaceuticals, Inc., Novo Nordisk A/S, OPKO Health, Inc., Roche Holding AG, and Takeda Pharmaceutical Company.

We believe we are the first and only company developing CAAR T drug candidates for the treatment of B cell-mediated autoimmune diseases. However, despite the significant differences in discovery, development and target populations between oncology and autoimmune targets, we recognize that companies with an investment and expertise in CAR T cell development for oncology indications could attempt to leverage their expertise into B cell-mediated autoimmune disease-affected populations. We are aware of biotechnology companies that are exploring other methods of engineering T cells for the treatment of autoimmune conditions. In addition, some biotechnology companies are engineering red blood cells to incorporate self-antigens with the goal of tolerizing the immune system to treat autoimmune and alloimmune conditions.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industry may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Intellectual Property and Barriers to Entry

We strive to protect the proprietary technologies that we believe are important to our business, including pursuing and maintaining patent protection intended to cover our product candidates and their use, as well as other inventions that are important to our business. In addition to patent protection, we also rely on know-how, confidentiality agreements, invention assignment agreements and trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection, to develop and maintain our proprietary position. The confidentiality agreements are designed to protect our proprietary information and the invention assignment agreements are designed to grant us ownership of technologies that are developed for us by our employees, consultants or certain other third parties. We seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in our agreements and security measures, either may be breached, and we may not have adequate remedies. In addition, our trade secrets may otherwise become known or independently discovered by competitors.

Our commercial success depends in part upon our ability to obtain and maintain patent and other proprietary protection for commercially important technologies, inventions and trade secrets related to our business, defend and enforce our intellectual property rights, particularly our patent rights, preserve the confidentiality of our trade secrets and operate without infringing valid and enforceable intellectual property rights of others.

The patent positions for biotechnology companies like us are generally uncertain and can involve complex legal, scientific and factual issues. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any of our product candidates will be protectable or remain protected by enforceable patents. 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.

As of March 1, 2022, our patent estate (all of which has been in-licensed) included one issued U.S. patent, two granted foreign patents, nine pending U.S. patent applications, and 43 pending foreign patent applications. See "—

Our Material Agreements—Amended and Restated License Agreement with the Trustees of the University of Pennsylvania and the Children's Hospital of Philadelphia."

With regard to our DSG3-CAART and DSG3/1-CAART product candidates, we have one issued U.S. patent with claims directed to a genetically modified cell containing a chimeric autoantibody receptor containing an extracellular domain containing DSG3, DSG1 or fragments thereof, which is scheduled to expire in 2035, without taking a potential patent term extension into account. We also have four pending U.S. patent applications and counterpart patents granted in Europe and China, which are scheduled to expire in 2035, and patent applications pending in Canada, China and Europe. This patent family is owned by Penn and exclusively licensed to us in the field of the license.

With regard to our MuSK-CAAR T cell product candidate, we have one pending U.S. patent application and counterpart patent applications pending in Australia, Canada, China, Europe, Israel, Japan, Korea, Mexico, New Zealand, and Russia, which if issued, would be expected to expire in 2039. This patent family is owned by Penn and exclusively licensed to us in the field of the license.

With regard to our PLA2R-CAAR T cell product candidate, we have two pending U.S. patent applications and counterpart patent applications pending in Australia, Canada, China, Europe, Israel, Japan, Korea, Mexico, New Zealand, and Russia, which if issued, would be expected to expire in 2039. This patent family is owned by Penn and exclusively licensed to us in the field of the license.

With regard to our FVIII-CAAR T cell product candidate, we have one pending U.S. patent application and counterpart patent applications pending in Australia, Canada, China, Europe, Japan, Hong Kong, Korea, Mexico, New Zealand, and Russia, which if issued, would be expected to expire in 2037. This patent family is co-owned by Penn and CHOP and is exclusively licensed to us in the field of the license.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the United States, the term of a patent covering an FDA-approved drug may be eligible for a patent term extension under the Hatch-Waxman Act as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years beyond the expiration of the patent, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension may be extended, and a given patent may only be extended once. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that issued U.S. patents covering each of our product candidates may be entitled to patent term extensions. If our product candidates receive FDA approval, we intend to apply for patent term extensions, if available, to extend the term of patents that cover the approved product candidates. We also intend to seek patent term extensions in any jurisdictions where they are available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we also rely on know-how and trade secret protection for our proprietary information that is not amenable to, or that we do not consider appropriate for, patent protection, to develop and maintain our proprietary position. However, trade secrets can be difficult to protect. Although we take steps to protect our proprietary information, including restricting access to our premises and our confidential information, as well as entering into agreements with our employees, consultants, advisors and potential collaborators, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our know-how, trade secrets, and other proprietary information.

In addition, we plan to rely on regulatory protection based on orphan drug exclusivities, data exclusivities, and market exclusivities. See "—Government Regulation" for additional information.

Our Material Agreements

Amended and Restated License Agreement with the Trustees of the University of Pennsylvania and the Children's Hospital of Philadelphia

In July 2019, we entered into an amended and restated license agreement, or the License Agreement, as further amended in May 2020 and October 2021, with Penn and CHOP, collectively the Institutions, pursuant to which we obtained (a) a non-exclusive, non-sublicensable, worldwide research license to make, have made and use products in two subfields of use, (b) effective as of October 2018, an exclusive, worldwide, royalty-bearing license, with the right to sublicense, under certain patent rights of the Institution to make, use, sell, offer for sale and import products in the same two subfields of use, and (c) effective as of October 2018, a non-exclusive, worldwide, royalty-bearing license, with limited rights to sublicense, under certain of Penn's know-how, which know-how satisfies certain criteria and is listed on a mutually agreed-to schedule, to make, have made, use, sell, offer for sale, import and have imported products in the same two subfields of use. Our rights are subject to the rights of the U.S. government and certain rights retained by the Institutions. The License Agreement was amended in May 2020 to add certain intellectual property relating to one of the two undisclosed disease targets and in October 2021 to extend certain dates by which we must achieve certain financial and regulatory milestones.

Unless earlier terminated, the License Agreement expires on the expiration or abandonment or other termination of the last valid claim in the intellectual property we license from Penn. We may terminate the License Agreement at any time for convenience upon 60 days written notice. In the event of an uncured, material breach, Penn may terminate the License Agreement upon 60 days written notice.

Penn maintains control of all filing, prosecution and maintenance of the Institutions' patent rights licensed by us, and we are responsible for all ongoing patent costs during the term of the agreement. We also reimbursed Penn for its out-of-pocket expenses incurred prior to the effective date of the agreement with respect to the filing, prosecution and maintenance of the patent rights licensed by us. Under the terms of the License Agreement, we were also obligated to pay $2.0 million annually for three years beginning August 2018 for funding to the laboratories of each of Drs. Milone and Payne. See "—Sponsored Research Agreements with the Trustees of the University of Pennsylvania."

Under the License Agreement, we must use commercially reasonable efforts to develop and commercialize a product in each subfield. During the term of the License Agreement until the first commercial sale of the first product, we are obligated to pay Penn a non-refundable, non-creditable annual license maintenance fee of $10,000. We are required to pay certain milestone payments upon the achievement of specified clinical and commercial milestones. Milestone payments are reduced by a certain percentage for the second product that achieves a milestone, by an additional percentage for the third product that achieves a milestone, and so on, for each subsequent product that achieves a milestone. In the event that we are able to successfully develop and launch multiple products under the License Agreement, total milestone payments could be approximately $21.0 million. Penn is also eligible to receive tiered royalties at percentage rates in the low single-digits, subject to an annual minimum royalty, on annual worldwide net sales of any products that are commercialized by us, our affiliates or our sublicensees that contain, use, embody, result from the use of or incorporate, or are covered by, the intellectual property licensed by us. To the extent we sublicense our license rights under the License Agreement, Penn would be eligible to receive tiered sublicense income at percentage rates in the mid-single to low double-digits. We have also entered into a subscription and technology transfer agreement with Penn, pursuant to which we owed Penn an upfront subscription fee, which was paid in 2019, and a nominal non-refundable royalty on the net sales of products, a portion of which will be credited toward milestone payments and royalties under this License Agreement. Technology transfer activities would be at our cost and subject to agreement as to the technology to be transferred.

Sponsored Research Agreements with Penn

Dr. Michael Milone

In April 2018, we entered into a Sponsored Research Agreement with Penn for the laboratory of Dr. Milone, or the Milone SRA, pursuant to which we agreed to sponsor certain research related to the development of (i) T cell based immunotherapies for autoimmune and alloimmune antibodies of pathologic significance and (ii) a clinical grade microfluidic device designed for single step selection and activation of T cells from blood samples to be conducted in Dr. Milone's laboratory at Penn. Under the Milone SRA, Penn granted us a perpetual, irrevocable, non-transferable, non-exclusive license to use all intellectual property resulting from the research sponsored by us for internal research purposes. In addition, Penn granted us an option to include, in exchange for a fee, any intellectual property resulting from the research sponsored by us that relates to CAAR T cell therapies for hemophilia and/or pemphigus within the

scope of the License Agreement. Penn also granted us an option to negotiate a license to all other intellectual property resulting from the research sponsored by us.In April 2021 and October 2021, the Milone SRA was amended to extend the term of the original research plan. Unless earlier terminated, the Milone SRA will expire in November 2022.

Dr. Aimee Payne

In April 2018, we entered into a Sponsored Research Agreement, or SRA, with Penn for the laboratory of Dr. Payne, or the Payne SRA, pursuant to which we agreed to sponsor certain research related to the development of T cell based immunotherapies for autoimmune and alloimmune antibodies of pathologic significance to be conducted in Dr. Payne's laboratory at Penn. In May 2020, the Payne SRA was amended to include CAAR design and optimization efforts in three additional B cell-mediated autoimmune diseases. In August 2020, this agreement was further amended to extend the term of the original research plan. In December 2021, we further amended the Payne SRA to extend the term and expand the workplan to include additional correlative studies related to the DesCAARTes ™ trial. Under the Payne SRA, Penn granted us a perpetual, irrevocable, non-transferable, non-exclusive license to use all intellectual property resulting from the research sponsored by us for internal research purposes. In addition, Penn granted us an option to include, in exchange for a fee, any intellectual property resulting from the research sponsored by us that relates to CAAR T cell therapies for hemophilia, MG and/or pemphigus within the scope of the License Agreement. Penn also granted us an option to negotiate a license to all other intellectual property resulting from the research sponsored by us. Unless earlier terminated, the Payne SRA will expire in December 2024.

We have estimated the total cost of the two SRAs to be $12.5 million, which satisfies the $2.0 million annual obligation under the License Agreement. As of December 31, 2021, $9.9 million of cost has been incurred pursuant to the Milone and Payne SRAs.

Dr. Drew Weissman

In December 2021, we entered into a SRA with Penn for the laboratory of Dr. Drew Weissman, or the Weissman SRA. Under the Weissman SRA, discovery-stage proof of concept studies for lipid nanoparticle mRNA for the delivery and/or enhancement of CAAR technology is being conducted. Under the Weissman SRA, Penn granted us a non-transferable, non-exclusive license to use certain intellectual property for specific internal research purposes and further grants us the first option to negotiate to acquire, subject to agreement on commercial terms, an exclusive or non-exclusive worldwide license to certain patent rights for specific CAAR products developed under the Weissman SRA. Unless earlier terminated, the Weissman SRA will expire in December 2023. Pursuant to the Weissman SRA, we also entered into an Option Agreement with Penn, or the Weissman Option, which grants us the option to negotiate to acquire a non-exclusive worldwide license to certain patent rights in connection with the Weissman SRA.

Master Translational Research Services Agreement with Penn

In October 2018, we entered into a Master Translational Research Services Agreement with Penn, or the Services Agreement, pursuant to which Penn agreed to perform certain services related to the research and development of the technology licensed to us under the License Agreement, as well as certain clinical, regulatory and manufacturing services. The Services Agreement will expire on the later of (i) October 19, 2021 or (ii) completion of the services for which we have engaged Penn under the Services Agreement. Either party may terminate this agreement with or without cause upon a certain number of days' prior written notice. The services encompassed by the Services Agreement are performed by different organizations at Penn pursuant to certain addenda to the Services Agreement, including the Center for Advanced Retinal and Ocular Therapeutics, or CAROT, Addendum, as amended in May 2020, and the CVPF Addendum. In addition, in July 2019 we entered into an Alliance Agreement with Penn, pursuant to which we will pay Penn a nominal annual fee in order for Penn to provide an adequate and consistent level of support to the services that it provides to us.

The CAROT Addendum

Under the CAROT Addendum, Penn manufactures vector that is then to be used by the CVPF in the manufacture of our product candidates. In the event that certain materials owned by Penn are incorporated into a product developed for us, Penn has agreed to grant us a limited license to use those materials. Further, Penn agreed to grant us an exclusive, paid-up, royalty-free, transferable, irrevocable, perpetual exclusive license to any deliverables produced under the CAROT Addendum, except with respect to certain technical information of Penn that is contained or

incorporated in the deliverables, to which Penn agreed to grant us a limited nonexclusive license. However, any necessary technology transfer would be pursuant to the subscription and technology transfer agreement described above.

The CVPF Addendum

Under the CVPF Addendum, Penn conducts process validation studies and large-scale engineering runs for our product candidates. Under the CVPF Addendum, CVPF will contractually agree to manufacture agreed upon quantities of DSG3-CAART material for use in connection with our DesCAARTes ™ trial, unless the agreement is terminated by either party. Any necessary technology transfer would be pursuant to the subscription and technology transfer agreement described above.

Government Regulation

U.S. Regulation

As a biopharmaceutical company that operates in the United States, we are subject to extensive regulation. Our cell products will be regulated as biologics. With this classification, commercial production of our products will need to occur in registered facilities in compliance with cGMP for biologics. The FDA categorizes human cell- or tissue-based products as either minimally manipulated or more than minimally manipulated, and has determined that more than minimally manipulated products require clinical trials to demonstrate product safety and efficacy and the submission of a BLA for marketing authorization. Our products are considered more than minimally manipulated and will require evaluation in clinical trials and the submission and approval of a BLA before we can market them.

Government authorities in the United States (at the federal, state and local level) and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of biopharmaceutical products such as those we are developing. Our product candidates must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agency before they may be legally marketed in foreign countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in Europe are addressed in a centralized way, but country-specific regulation remains essential in many respects. The process for obtaining regulatory marketing approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Biological Product Development

In the United States, the FDA regulates biologics under the Federal Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHSA, and their implementing regulations. Biologics are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may result in delays to the conduct of a study, regulatory review and approval or subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, license suspension or revocation, refusal to allow an applicant to proceed with clinical trials, imposition of a clinical hold, issuance of untitled or warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations or penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Our drug product candidates must be approved by the FDA through the Biologics License Application, or BLA, process before they may be legally marketed in the United States. The process required by the FDA before a biologic may be marketed in the United States generally involves the following:

- completion of extensive nonclinical, sometimes referred to as preclinical, laboratory tests, animal studies and formulation studies in accordance with applicable regulations, including the FDA's Good Laboratory Practice, or GLP, regulations and standards;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practices, or GCPs, and other clinical trial-related regulations to establish the safety and efficacy of the proposed drug product candidate for its proposed indication;
- submission to the FDA of a BLA, which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labeling;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the product is produced to assess compliance with the FDA's current good manufacturing practice, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality, purity and potency;
- potential FDA audit of the preclinical trial sites and/or clinical trial sites that generated the data in support of the BLA; and
- FDA review and approval of the BLA prior to any commercial marketing or sale of the product in the United States.

The data required to support a BLA is generated in two distinct development stages: preclinical and clinical. The preclinical development stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The conduct of the preclinical studies must comply with federal regulations, including GLPs. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, as well as other information, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug product candidate at any time before or during clinical trials due to safety concerns, non-compliance, or other issues affecting the integrity of the trial. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

In addition to the submission of an IND to the FDA before initiation of a clinical trial in the United States, certain human clinical trials involving recombinant or synthetic nucleic acid molecules are subject to oversight of institutional biosafety committees, or IBCs, as set forth in the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. Under the NIH Guidelines, recombinant and synthetic nucleic acids are defined as: (i) molecules that are constructed by joining nucleic acid molecules and that can replicate in a living cell (i.e., recombinant nucleic acids); (ii) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules (i.e., synthetic nucleic acids); or (iii) molecules that result from the replication of those described in (i) or (ii). Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being

conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

The clinical stage of development involves the administration of the drug product candidate to healthy volunteers and patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an IRB at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products, including biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov.

Clinical trials are generally conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap. Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the drug product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action tolerability, adverse effects, and safety of the drug product candidate and, if possible, to gain early evidence on effectiveness. Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy. Phase 3 clinical trials generally involve large numbers of patients at multiple sites, in multiple countries, and are designed to provide the data necessary to demonstrate the efficacy of the product for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of a BLA. In certain instances, FDA may condition approval of a BLA on the sponsor's agreement to conduct additional clinical trials to further assess the biologic's safety and effectiveness after BLA approval. Such post-approval trials are sometimes referred to as Phase 4 clinical trials. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and further document clinical benefit in the case of drugs approved under Accelerated Approval regulations. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the biologic, findings from animal or in vitro testing that suggest a significant risk for human subjects, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated intervals based on access to certain data from the trial and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as interim data suggesting a lack of efficacy. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug product candidate as well as 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 drug product candidate and, among other things, must develop methods for testing the identity, strength,

quality, potency and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug product candidate does not undergo unacceptable deterioration over its shelf life.

BLA and FDA Review Process

Following trial completion, trial data are analyzed to assess safety and efficacy. The results of preclinical studies and clinical trials are then submitted to the FDA as part of a BLA, along with proposed labeling for the product and information about the manufacturing process and facilities that will be used to ensure product quality, results of analytical testing conducted on the chemistry of the drug product candidate, and other relevant information. The BLA is a request for approval to market the biologic for one or more specified indications and must contain proof of safety, purity, potency and efficacy, which is demonstrated by extensive preclinical and clinical testing. The application may include both negative or ambiguous results of preclinical and clinical trials as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. FDA approval of a BLA must be obtained before a biologic may be marketed in the United States.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a significant user fee, which is adjusted on an annual basis. PDUFA also imposes an annual prescription drug product program fee. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business.

Once a BLA has been accepted for filing, which occurs, if at all, sixty days after the BLA's submission, the FDA's goal is to review BLAs within 10 months of the filing date for standard review or six months of the filing date for priority review, if the application is for a product intended for a serious or life-threatening condition and the product, if approved, would provide a significant improvement in safety or effectiveness. The FDA has substantial discretion in the approval process and may refuse to accept any application or decide that the data is insufficient for approval, and may require additional preclinical, clinical or other studies before it accepts the filing. Additionally, the review process is often significantly extended by FDA requests for additional information or clarification.

After the BLA submission is accepted for filing, the FDA reviews the BLA to determine, among other things, whether the proposed drug product candidate is safe and effective for its intended use, and whether the drug product candidate is being manufactured in accordance with cGMP to assure and preserve the drug product candidate's identity, strength, quality, purity and potency. The FDA may refer applications for novel drug product candidates or drug product candidates which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and us during the review process. The review and evaluation of a BLA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

Before approving a BLA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether the facilities comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving a BLA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities, it 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 indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the BLA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, withdraw

the application or request a hearing. Even if such data and information is submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a product for marketing in the United States, and we may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific populations, severities of allergies, and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the BLA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 testing which involves clinical trials designed to further assess the product's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a Risk Evaluation and Mitigation Strategy, or REMS, to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS. The FDA will not approve the BLA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or based on the results of post-market studies or surveillance programs. Additionally, post-approval, many types of changes to the approved product, such as adding new indications, changing manufacturing processes and adding labeling claims, are subject to further testing requirements and FDA review and approval. Such post-approval requirements can be costly and time-consuming and can affect the potential market and profitability of the product.

Orphan Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug or biologic for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity on the basis of greater effectiveness or safety or providing a major contribution to patient care or in instances of drug supply issues. Competitors, however, may receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if our product is determined to be contained within the scope of the competitor's product for the same indication or disease. If we pursue marketing approval for an indication broader than the orphan drug designation we have received, we may not be entitled to orphan drug exclusivity. Orphan drug status in the European Union has similar, but not identical, requirements and benefits.

Expedited Development and Review Programs

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for fast

track designation if they are intended to treat a serious or life-threatening condition and nonclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a fast track product concurrently with, or at any time after, submission of an IND, and the FDA must determine if the product qualifies for fast track designation within 60 days of receipt of the sponsor's request. Under the fast track designation, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review, or review within a six-month timeframe from the date a complete BLA is accepted for filing, if it has the potential to provide a significant improvement in safety and effectiveness compared to available therapies. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review.

Additionally, a product may be eligible for accelerated approval. An investigational drug may obtain accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies and demonstrates 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, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it will require such post-marketing restrictions as it deems necessary to assure safe use of the drug, such as:

- distribution restricted to certain facilities or physicians with special training or experience; or
- distribution conditioned on the performance of specified medical procedures.

The limitations imposed would be commensurate with the specific safety concerns presented by the product. 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. Fast track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

Breakthrough Designation

A product can be designated as a breakthrough therapy if it is intended to treat a serious or life-threatening condition and preliminary clinical evidence indicates that it may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A sponsor may request that a drug product candidate be designated as a breakthrough therapy concurrently with, or at any time after, the submission of an IND, and the FDA must determine if the drug product candidate qualifies for breakthrough therapy designation within 60 days of receipt of the sponsor's request. If so designated, the FDA shall act to expedite the development and review of the product's marketing application, including by meeting with the sponsor throughout the product's development, providing timely advice to the sponsor to ensure that the development program to gather preclinical and clinical data is as efficient as practicable, involving senior managers and experienced review staff in a cross-disciplinary review, assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor, and taking steps to ensure that the design of the clinical trials is as efficient as practicable.

Accelerated Approval for Regenerative Medicine Advanced Therapies

FDA's regenerative medicine advanced therapy (RMAT) program is intended to facilitate efficient development and expedite review of regenerative medicine advanced therapies, which are intended to treat, modify, reverse, or cure

a serious or life-threatening disease or condition. A drug sponsor may request that FDA designate a drug as an RMAT concurrently with or at any time after submission of an IND. FDA has 60 calendar days to determine whether the drug meets the criteria, including whether there is preliminary clinical evidence indicating that the drug has the potential to address unmet medical needs for a serious or life-threatening disease or condition. A BLA for an RMAT may be eligible for priority review or accelerated approval through (1) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit or (2) reliance upon data obtained from a meaningful number of sites. Benefits of such designation also include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. An RMAT that is granted accelerated approval and is subject to post approval requirements may fulfill such requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post approval monitoring of all patients treated with such therapy prior to its approval.

Pediatric Trials

Under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and efficacy of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDCA requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of data or full or partial waivers.

Post-Marketing Requirements

Following approval of a new product, a manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the product, providing the regulatory authorities with updated safety and efficacy information, product sampling, distribution, and tracking and tracing requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs and biologics for off-label uses, manufacturers may not market or promote such off-label uses.

Modifications or enhancements to the product or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, which may or may not be received or may result in a lengthy review process. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use.

In the United States, once a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP regulations require, among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. These regulations also impose certain

organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. BLA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including, among other things, recall or withdrawal of the product from the market.

The FDA also may require post-approval testing, sometimes referred to as Phase 4 testing, REMS and post-marketing surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, untitled or warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Other Regulatory Matters

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, or CMS, other divisions of the Department of Health and Human Services, or HHS (e.g., the Office of Inspector General, or OIG, and Office for Civil Rights), the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments. In the United States, sales, marketing and scientific/educational programs must also comply with federal and state fraud and abuse laws, data privacy and security laws, transparency laws, and pricing and reimbursement requirements in connection with governmental payor programs, among others. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

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

The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or efficacy of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of our drug product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to 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. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

An abbreviated approval pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed reference biological product was created by the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, which was part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA. This amendment to the PHSA attempts to minimize duplicative testing. Biosimilarity, which requires that the biological product be highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there be no clinically meaningful differences between the product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a biological product be biosimilar to the reference product and that the product can be expected to produce the same clinical results as the reference product in any given patient and, for products administered multiple times, that the product and the reference product may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product. However, complexities associated with the larger, and often more complex, structure of biological products as compared to small molecule drugs, as well as the processes by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

A reference biological product is granted twelve years of exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after first licensure. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. This does not include a supplement for the biological product or a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength, unless that change is a modification to the structure of the biological product and such modification changes its safety, purity, or potency. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which attaches to the twelve-year exclusivity period for reference biologics, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

Pricing and Reimbursement

United States

Sales of our products will depend, in part, on the extent to which our products, once approved, will be covered and reimbursed by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for medical products and services. The process for determining whether a third-party payor will provide coverage for a drug product, including a biologic, typically is separate from the process for setting the price of a drug product or for establishing the reimbursement rate that a payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the approved drugs for a particular indication.

In order to secure coverage and reimbursement for any drug product candidate that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the drug product candidate, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Whether or not we conduct such studies, our drug product candidates may not be considered medically necessary or cost-effective. A third-party payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development. In the United States, the principal decisions about reimbursement for new drug products are typically made by CMS, an agency within HHS. CMS decides whether and to what extent a new drug product will be covered and reimbursed under Medicare, and private payors tend to follow CMS to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists among third-party payors and coverage and reimbursement levels for drug products can differ significantly from payor to payor. Additionally, one third-party payor's decision to cover a particular product or service does not ensure that other payors will also provide coverage for the product or service, and the level of coverage and reimbursement can differ significantly from payor to payor. As a result, the coverage determination process will often require us to provide scientific and clinical support for the use of our products to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

The containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs, including biologics, have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. In many countries, the prices of drug products are subject to varying price control mechanisms as part of national health systems. In general, the prices of drug products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for drug products, but monitor and control company profits. Accordingly, in markets outside the United States, the reimbursement for drug products may be reduced compared with the United States. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our drug product candidate or a decision by a third-party payor to not cover our drug product candidate could reduce physician usage of the drug product candidate and have a material adverse effect on our sales, results of operations and financial condition.

Outside of the United States, the pricing of pharmaceutical products is subject to governmental control in many countries. For example, in the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been approved. Some countries may require the completion of additional studies that compare the cost effectiveness of a particular therapy to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. Other countries may allow companies to fix their own prices for products, but monitor and control product volumes and issue guidance to physicians to limit prescriptions. Efforts to control prices and utilization of pharmaceutical products will likely continue as countries attempt to manage healthcare expenditures.

Other Healthcare Laws and Compliance Requirements

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations in the United States and our current and future arrangements with clinical investigators, healthcare providers, consultants, third-party payors and patients may expose us to broadly applicable federal and state fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. In the United States, these laws include: the federal Anti-Kickback Statute, the False Claims Act, and HIPAA.

The Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration, directly or indirectly, in cash or in kind, that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by imprisonment, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

Although we would not submit claims directly to payors, drug manufacturers can be held liable under the federal civil False Claims Act, which imposes civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities (including manufacturers) for, among other things, knowingly presenting, or causing to be presented to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties for each separate false claim, the potential for exclusion from participation in federal healthcare programs and, although the federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. The government may deem manufacturers to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off- label. Claims which include items or services resulting from a violation of the federal Anti-Kickback Statute are false or fraudulent claims for purposes of the False Claims Act. Our future marketing and activities relating to the reporting of wholesaler or estimated retail prices for our products, if approved, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our product candidates, are subject to scrutiny under this law.

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

Additionally, we may be subject to data privacy and security regulations by both the federal government and states in which we conduct our business. For example, HIPAA created new federal criminal statutes that prohibit among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the federal Anti-Kickback Statute a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

HIPAA, as amended by HITECH, and their implementing regulations, mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, defined as independent contractors or agents of covered entities, which include certain health care providers, health plans, and healthcare clearinghouses, that create, receive or obtain protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities and business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, certain state laws govern the privacy and security of health information and other personal data in certain circumstances, some of which are more stringentor otherwise different than HIPAA and 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 criminal penalties.

Further, the federal Physician Payments Sunshine Act, or the Sunshine Act, within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, physicians, certain other healthcare professionals, and teaching hospitals and to report annually certain ownership and investment interests held by physicians, certain other healthcare professionals, and their immediate family members. Effective January 1, 2022, these reporting obligations extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners. In addition, many states also govern the reporting of payments or other transfers of value, many of which differ from each other in significant ways, are often not pre-empted, and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts.

We may become subject to federal government price reporting laws, which would require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs, as well as federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Similar federal, state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services. Such laws are generally broad and are enforced by various state agencies and private actions. Also, many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant federal government compliance guidance, and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures.

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

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations 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 these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, individual imprisonment, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource- consuming and can divert a company's attention from the business.

Current and Future Legislation

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare.

For example, in March 2010, the ACA was enacted in the United States. The ACA includes measures that have significantly changed, and are expected to continue to significantly change, the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA of greatest importance to the pharmaceutical industry are that the ACA:

1. made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on average manufacturer price, or AMP, on most branded prescription drugs and adding a new rebate calculation for "line extensions" (*i.e.*, new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP;
2. imposed a requirement on manufacturers of branded drugs to provide a 50% point-of-sale discount (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of January 1, 2019) off the negotiated price of branded drugs dispensed to Medicare Part D beneficiaries in the coverage gap (*i.e.*, "donut hole") as a condition for a manufacturer's outpatient drugs being covered under Medicare Part D;
3. extended a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
4. expanded the entities eligible for discounts under the 340B Drug Discount Program;
5. established 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;
6. imposed an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs, apportioned among these entities according to their market share in certain government healthcare programs, and
7. established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products. The ACA established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation through 2019.

Since its enactment, there have been judicial, Congressional and executive challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the 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 from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental 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. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal or replace the ACA will impact our business. Other legislative changes have been proposed and adopted in the United States since the ACA was enacted:

- In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013, following passage of the Bipartisan Budget Act of 2013 and subsequent legislation, and will remain in effect through 2030 unless additional congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, the 2% Medicare sequester reductions have been suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Following the temporary suspension, a 1% payment reduction will occur beginning April 1, 2022 through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022.

- In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability. Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. On May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to request access to certain IND products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

- On April 13, 2017, CMS published a final rule that gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

- On May 23, 2019, CMS published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020.

- On December 20, 2019, former President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repealed the Cadillac tax, the health insurance provider tax, and the medical device excise tax. It is impossible to determine whether similar taxes could be instated in the future.

In addition, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient assistance programs, and reform government program reimbursement methodologies for drugs. At the federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and

biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates would have been be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. However, on December 29, 2021 CMS rescinded the Most Favored Nations rule. Additionally, on November 30, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and 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, financial condition, results of operations 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 drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

We cannot predict what healthcare reform initiatives may be adopted in the future. Further federal, state and foreign legislative and regulatory developments are likely, and we expect ongoing initiatives to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates and may affect our overall financial condition and ability to develop product candidates.

The Foreign Corrupt Practices Act

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

Additional Regulation

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

Europe / Rest of World Government Regulation

In addition to regulations in the United States, we may be subject to a variety of regulations in other jurisdictions that we may in the future select governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we obtain FDA approval of a product, we would need to obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the EU, for example, a clinical trial application must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the clinical trial application is approved in accordance with a country's requirements, clinical trial development may proceed. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological product under EU regulatory systems, we must submit an MAA. The application used to file the BLA in the United States is similar to that required in the EU, with the exception of, among other things, country-specific document requirements.

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

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

European Union General Data Protection Regulation

In addition to EU regulations related to the approval and commercialization of our products, we may be subject to the EU's General Data Protection Regulation, or GDPR. The GDPR imposes stringent requirements for controllers and processors of personal data of persons in the EU, including, for example, more robust disclosures to individuals and a strengthened individual data rights regime, shortened timelines for data breach notifications, limitations on retention of information, increased requirements pertaining to special categories of data, such as health data, and additional obligations when we contract with third-party processors in connection with the processing of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States and other third countries. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

The GDPR applies extraterritorially, and we may be subject to the GDPR because of our data processing activities that involve the personal data of individuals located in the European Union, such as in connection with our EU clinical trials. Failure to comply with the requirements of the GDPR and the applicable national data protection laws of the EU member states may result in fines of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, and other administrative penalties. GDPR regulations may impose additional responsibility and liability in relation to the personal data that we process and we may be required to put in place additional mechanisms to ensure compliance with the new data protection rules.

Human Capital Management

As of December 31, 2021, we had 54 employees, 53 of whom were full-time and one who was part-time. Of those, 45 were engaged in research and development activities. All company employees are located in the United States. We do not have any employees that are represented by a labor union or covered under a collective bargaining agreement. We consider our relationship with our employees to be good.

Our future success depends on our ability to attract, develop and retain key personnel, maintain our culture, and ensure diversity and inclusion in our board, management and broader workforce. Our human resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards. As these areas directly impact our ability to compete and innovate, they are key focus areas for our board of directors and senior executives. A testament to our strong culture is the strong results from our annual employee survey.

Corporate History and Trademarks

We were incorporated under the laws of the State of Delaware in April 2017 under the name Tycho Therapeutics, Inc. In August 2018, our corporate name was changed to Cabaletta Bio, Inc. Our principal executive offices are located at 2929 Arch Street, Suite 600, Philadelphia, PA 19104 and our telephone number is (267) 759-3100. Our website address is www.cabalettabio.com. We do not incorporate the information on or accessible through our website into this Annual Report on Form 10-K, and you should not consider any information on, or that can be accessed through, our website to be part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

We view our operations and measure our business as one reportable segment. All of the Company's tangible assets are held in the United States. Refer to Note 2, Summary of Significant Accounting Policies, to our financial statements appearing elsewhere in this Annual Report on Form 10-K for additional information.

We own or have rights to various trademarks, service marks and trade names that we use in connection with the operation of our business. This Annual Report on Form 10-K may also contain trademarks, service marks and trade names of third parties, which are the property of their respective owners. Our use or display of third parties' trademarks, service marks, trade names or products in this Annual Report on Form 10-K is not intended to, and does not imply a relationship with, or endorsement or sponsorship by us. Solely for convenience, the trademarks, service marks and trade names referred to in this Annual Report on Form 10-K may appear without the ®, ™ or SM symbols, but the omission of such references is not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the right of the applicable owner of these trademarks, service marks and trade names.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge on our website located at www.cabalettabio.com as soon as reasonably practicable after they are filed with or furnished to the SEC. These reports are also available at the SEC's Internet website at www.sec.gov.

A copy of our Corporate Governance Guidelines, Code of Conduct and Business Ethics and the charters of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are posted on our website, www.cabalettabio.com, under the heading "Investors & Media."

Item 1A. Risk Factors.

Our business involves material and other risks, some of which are summarized and described below. You should carefully consider the risks and uncertainties described below, together with all of the other information contained in this Annual Report on Form 10-K, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the condensed financial statements and the related notes. If any of the following risks actually occur, it could harm our business, prospects, operating results and financial condition and future prospects. In such event, the market price of our common stock could decline and you could 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. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Annual Report.

Risks Related to Our Business, Technology and Industry

Risks Related to Clinical Development

We are early in our development efforts. If we are unable to advance our product candidates through clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts and we have not yet completed any clinical trials. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. Even if we are able to develop and commercialize a marketable product, we may face challenges generating revenue from product sales. The success of our product candidates will depend on several factors, including the following:

- successful completion of preclinical studies resulting in data that is supportive of advancing to an IND submission;
- successful submission and acceptance of INDs or comparable applications;
- successful initiation of clinical trials;
- demonstration of adequate safety to progress to a therapeutic dose level;
- successful patient enrollment in and completion of clinical trials;
- receipt and related terms of regulatory and marketing approvals and licensures from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers for clinical supply and commercial manufacturing of our product candidates;
- making arrangements with various medical divisions across hospitals for administration of our product candidates, including with cancer treatment centers to conduct leukapheresis and with the relevant hospital divisions to perform infusion;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- establishing sales, marketing and distribution and patient administration capabilities and launching commercial sales of our products, if and when licensed, whether alone or in collaboration with others;
- acceptance of our products, if and when licensed, by patients, the medical community and third-party payors;
- effectively competing with other therapies targeting the same indications as our product candidates;
- obtaining and maintaining third-party coverage and adequate reimbursement; and
- maintaining a continued acceptable safety profile of our products following licensure.

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

Cellular therapies, including our engineered chimeric autoantibody receptor, or CAAR, T cell product candidates, represent a novel approach to the treatment of B cell-mediated autoimmune diseases, which creates significant challenges for us. Negative perception or increased regulatory scrutiny of any product candidates that we develop could adversely affect our ability to conduct our business or obtain regulatory approvals for such product candidates.

Cellular therapies are a novel approach and negative perception or increased regulatory scrutiny of any product candidates that we develop could adversely affect our ability to conduct our business or obtain regulatory approvals for such product candidates. Cellular therapies in general, and CAAR T cell therapies in particular, remain novel therapies, with no cellular immunotherapies licensed to date in the United States or the European Union to treat autoimmune diseases or alloimmune responses. CAAR T cell therapies may not gain the acceptance of the public or the medical community. For example, CAR Ts and other cellular therapies have in some cases caused severe side effects, including death, and their broader use may therefore be limited. Even if CAR Ts and other cellular therapies are accepted by the public and medical community in the short term, long-term adverse events observed in these therapies may increase negative perception and regulatory scrutiny. Although our CAAR Ts are different from CAR Ts and other cellular therapies, they may be viewed in the same vein, limiting their market acceptance. Public perception may be influenced by claims that gene therapy, including the insertion of a transgene, is unsafe, and products incorporating gene therapy may not gain the acceptance of the public or the medical community. The patient populations targeted by our product candidates are also typically not at risk of near-term death, even if they may suffer life-threatening symptoms, so patients will need to deem the benefits of cell therapy to be worth the risk of unknown potential adverse side effects. Our success will depend upon physicians who specialize in the treatment of B cell-mediated autoimmune diseases targeted by our product candidates prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments with which they are more familiar and for which greater clinical data may be available. Adverse events in clinical trials of our product candidates or in clinical trials of others developing similar products and the resulting publicity, as well as any other adverse events in the field of cellular therapies, could result in a decrease in demand for any product that we may develop.

We are developing a pipeline of CAAR T product candidates that are intended for use in treating individuals with B cell-mediated autoimmune disease. Advancing these novel product candidates creates significant challenges for us, including:

- manufacturing our product candidates to our specifications and in a timely manner to support our clinical trials, and, if licensed, commercialization;
- sourcing clinical and, if licensed, commercial supplies for the materials used to manufacture our product candidates;
- understanding and addressing variability in the quality and quantity of a subject's T cells, which could ultimately affect our ability to manufacture clinical supply and, if licensed, commercial supply of our product candidates in a reliable and consistent manner;
- educating medical personnel regarding the potential side effect profile of our product candidates, if licensed, such as the potential adverse side effects related to pemphigus flare from infusion of activated T cells or medication taper, cytokine release syndrome, or CRS, or other unexpected adverse effects of therapy with our product candidates;
- facilitating patient access to the limited number of facilities able to administer our product candidates, if licensed;
- using medicines to manage adverse side effects of our product candidates that may not adequately control the side effects and/or may have a detrimental impact on the efficacy of the treatment;
- potentially utilizing preconditioning agents in patients to enhance engraftment in advance of administering our product candidates, which may increase the risk of adverse side effects;
- obtaining and maintaining regulatory approval for our product candidates, as the FDA and other regulatory authorities have limited or no experience with development of engineered T cell therapies for the treatment of B cell-mediated autoimmune diseases;

- establishing sales and marketing capabilities upon obtaining any regulatory approval to gain market acceptance of a novel therapy; and
- managing costs of inputs and other supplies while scaling production.

In addition, preclinical murine and other animal models may not exist or be adequate for some or all of the B cell-mediated autoimmune diseases we choose to pursue in our programs, and because we are early in the clinical development process, we are unable to predict whether there may be short-term or long-term effects from treatment with any product candidates that we develop. In developing our product candidates, we have not exhaustively explored different options in the method for manufacturing CAAR T cells. We may find our existing manufacturing process may be substantially improved with future design or process changes, necessitating further clinical testing, delaying commercial launch of our first products, and causing us to incur additional expenses. For example, while we have used a lentiviral vector in our manufacturing process, we may in the future find that another viral vector or non-viral vector-based process offers advantages. Switching from one lentiviral vector to another or switching from lentiviral to another delivery system would necessitate additional process development and clinical testing, and this may delay the development of existing product candidates.

In addition, we do not know the doses to be evaluated in pivotal trials or, if licensed, commercially. Finding a suitable dose may delay our anticipated clinical development timelines. Our expectations with regard to our scalability and costs of manufacturing may vary significantly as we develop our product candidates and understand these critical factors. We may experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical studies or commercializing our product candidates on a timely or profitable basis, if at all.

Moreover, our product candidates may not perform successfully in clinical trials or may be associated with adverse events that distinguish them from the chimeric antigen receptor T, or CAR T, therapies that have previously been licensed. For instance, subjects in our clinical trials will be infused with our proposed therapies, and may possess strongly activating soluble antibodies, which, are not present in oncology patients and when they interact with our infused product candidates, could result in potential adverse side effects, such as CRS. Unexpected side effects or clinical outcomes would significantly impact our business. Adverse side effects caused by even one of our product candidates could negatively affect our ability to develop future product candidates based on our CABA™ platform.

In addition, two of our current product candidates, DSG3/1-CAART and FVIII-CAART, and certain of our future product candidates may require introducing large transgenes into T cells, and lentiviral vectors may have too limited a genome capacity to accomplish this process. We currently use lentiviral vector transduction for transgene delivery. However, lentiviral vectors have a limited genome capacity that restricts the size of the transgene that can be delivered using this vector system. For example, designing a lentiviral vector that will have sufficient capacity to introduce DSG3 CAAR and DSG1 CAAR together into T cells may not be possible. In addition to reducing lentiviral vector titers that may substantially increase the cost of gene transfer, it may be entirely unsuccessful, thus necessitating use of alternative strategies for transfer of these larger transgenes into T cells.

Further, the clinical study requirements of the FDA and other regulatory agencies and the criteria they use to determine the safety, potency and purity of a product candidate are determined according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours is less clear, and can be more complex and consequently have higher development risk, be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. Approvals by the FDA for existing cell therapies treating B cell-mediated diseases, such as Kymriah (Novartis Pharmaceuticals Corporation) and Yescarta (Gilead Sciences, Inc.), may not be indicative of what the FDA may require for approval of our therapies. Approvals by any regulatory agency may not be indicative of what any other regulatory agency may require for approval or what such regulatory agencies may require for approval in connection with new product candidates. As we advance our product candidates, we will be required to consult with these regulatory agencies and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. More restrictive statutory regimes, government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop.

In addition, responses by agencies at the federal and state level to negative public perception or ethical concerns may result in new legislation or regulations that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval or otherwise achieve profitability. The FDA has expressed interest in further regulating biotechnology products, such as cellular therapies. Agencies at both the federal and state level in the United States, as well as the U.S. Congressional committees and other government entities or governing agencies have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some or all of our product candidates. Adverse developments in clinical trials of cellular therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any of our product candidates. These regulatory review agencies and committees and the new requirements or guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions.

Patients receiving T cell-based immunotherapies, such as our product candidates, may experience serious adverse events, including neurotoxicity, CRS and killing of cells other than the intended B cells that express the autoantibodies. If our product candidates are revealed to have high and unacceptable severity and/or prevalence of side effects or unexpected characteristics, their clinical development, regulatory approval, and commercial potential will be negatively impacted, which will significantly harm our business, financial condition and prospects.

Our product candidates are CAAR T cell-based immunotherapies. There is a possibility that our product candidates could have adverse side effects, such as neurotoxicity and CRS. In other similarly designed cellular immunotherapies to treat cancer, there have been life threatening events related to severe neurotoxicity and CRS requiring intense medical intervention, such as intubation or medications to support blood pressure, and in several cases, resulted in death. Severe neurotoxicity is a condition that is currently defined clinically by cerebral edema, confusion, drowsiness, speech impairment, tremors, seizures or other central nervous system side effects, when such side effects are serious enough to lead to intensive care. CRS is a condition that is currently defined clinically by certain symptoms related to the release of cytokines, which can include fever, chills and low blood pressure, when such side effects are serious enough to lead to intensive care with mechanical ventilation or significant medications to support blood pressure.

Our product candidates may have serious and potentially fatal consequences due to the targeting of cells within the body due to unexpected protein interactions with the CAAR. Although we have completed multiple preclinical studies designed to screen for toxicity caused by unintended off-target recognition by the cell binding domain of the DSG3 CAAR and MuSK CAAR, our product candidates may still recognize and react with one or more proteins unrelated to the intended surface immunoglobin target protein to which it is designed to link. If unexpected binding occurs in normal tissue, our product candidates may target and kill the normal tissue in a patient, leading to serious and potentially fatal adverse events, undesirable side effects, toxicities or unexpected characteristics. Detection of any unexpected targeting may halt or delay any ongoing clinical trials for our product candidates and prevent or delay regulatory approval. While we have developed a preclinical screening process to identify cross-reactivity of our product candidates, we cannot be certain that this process will identify all potential tissue that our product candidates may target. For example, a membrane protein array with DSG3-CAART yielded one weak signal against a protein that is designed to bind to glycoproteins and which was detected in both the test and control conditions. Further analysis of this protein in confirmatory cell-based assays repeatedly demonstrated that DSG3-CAART does not recognize nor activate against this protein. We performed similar preclinical studies for the MuSK CAAR and did not observe any confirmed off target activity for MuSK-CAART. However, this further analysis may prove to be inaccurate. Any unexpected targeting that impacts patient safety could materially impact our ability to advance our product candidates into clinical trials or to proceed to marketing approval and commercialization. Furthermore, in the event subjects are retreated, they may respond differently than other subjects given the same dose, and may not tolerate the dose or develop safety concerns.

Results of our studies could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory

approval by the FDA. The FDA has requested and we have agreed to provide data on the subjects dosed in Part A of our DesCAARTes™ trial prior to dosing subjects in Part B. The FDA has communicated that the dosing of patients in Part B1 is not dependent on the review of Part A data and that they will provide feedback, if any, in a timely manner. In some cases, side effects such as neurotoxicity or CRS have resulted in clinical holds of ongoing clinical trials and/or discontinuation of the development of the product candidate. Given that the autoimmune and alloimmune diseases we are seeking to treat are, in some cases, less serious than the later stage cancers being treated with other immunotherapy products, we believe the FDA and other regulatory authorities likely will apply a different benefit-risk assessment thresholds such that even if our product candidate demonstrated a similar safety profile as current CAR T therapies, the FDA may ultimately determine that the harmful side effects outweigh the benefits and require us to cease clinical trials or deny approval of our product candidates. We believe tolerance for adverse events in the patient population being pursued with CAAR T cell therapies will be lower than it is in oncology, and the risks of negative impact from these toxicities may therefore be higher for us than for CAR T programs in oncology.

Furthermore, treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the studies or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from T cell-based immunotherapies are not normally encountered in routine medical care. Medical personnel may need additional training regarding T cell-based immunotherapy product candidates to understand their side effects. Inadequate training in recognizing or failure to effectively manage the potential side effects of T cell-based immunotherapy product candidates could result in patient deaths. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition to side effects caused by our product candidates, any preconditioning, administration process or related procedures, which we evaluate from time to time as part of our process improvement and optimization efforts, may also cause adverse side effects. For example, severe neurotoxicity has been noted to be associated with the use of certain lymphodepleting regimens and CAR T therapies. While we believe there are sufficient data from other CAR T programs to suggest that it is reasonable for us to initiate our first clinical trial of DSG3-CAART without a preconditioning regimen, we cannot be certain that a preconditioning regimen, with or without lymphodepleting agents, will not be required.

Although we plan to infuse DSG3-CAART without preconditioning initially in our DesCAARTes™ trial, we may in the future use a preconditioning regimen for our CAAR T cell product candidates, which may increase the risk of adverse side effects and impact our ability to accurately assess the efficacy of our product candidates.

In oncology patients receiving CAR T cell therapy, a lymphodepleting preconditioning regimen is typically used to condition the patient prior to CAR T cell infusion in order to improve tumor immunogenicity and to promote the expansion of the infused CAR T cells. Together, these effects have been shown to enhance the clinical activity of CAR T cells in oncology patients. These regimens often include cyclophosphamide and fludarabine and are usually administered within the week prior to infusion of CAR T cells. Serious adverse events have been observed in some patients following CAR T cell infusion, and these include infection, cytokine release syndrome and neurotoxicity. The preconditioning regimen may contribute to the occurrence and severity of these adverse events due to its role in inducing lymphopenia, or low levels of lymphocytes in the blood, and enhanced CAR T cell activity.

Lymphodepleting preconditioning may not be required in all oncology settings for CAR T cell activity. A recent clinical trial in multiple myeloma patients published in 2019 in *The Journal of Clinical Investigation* showed similar clinical activity of CAR T cell infusions in patients with or without a lymphodepleting preconditioning regimen. Furthermore, the requirement for lymphodepleting preconditioning for potentiating engineered T cell therapy outside of oncology has not been well established. Specifically, the effect on tumor immunogenicity is not relevant in settings outside oncology, and therefore the contribution of this aspect to the potential enhancing effect of preconditioning would not apply.

In addition, a lymphodepleting regimen may eliminate pathogenic B cells targeted by our CAAR T cell product candidates. As a result, any lymphodepleting regimen for preconditioning that we use may adversely affect our ability to use DSG3 autoantibody titers, a standard clinical assay, to assess the activity of DSG3-CAART. An inability to use DSG3 autoantibody levels to demonstrate the specific activity of our CAAR T cell product candidates may require us to rely on the subjective measurement of blister formation in patients, which can be a less sensitive and accurate measurement of CAAR T cell activity. This therefore could delay a signal of potential biologic activity attributable to

CAAR and therefore efficient clinical development. As a result of these factors, including the concern that lymphodepletion may confer a potential increased safety risk to an autoimmune patient population, we believe the inclusion of such a regimen must be justified by clinical data demonstrating the need for it in the setting of autoimmune patients and is therefore difficult to justify in our first-in-human studies.

In addition to lymphodepleting preconditioning, other preconditioning regimens may be considered to prepare the body for CAAR T infusion. For example, if autoantibody is found to reduce or inhibit function of CAAR T in the body, then pretreatment of patients with antibody reducing therapies, such as FcRN inhibitors, IVIG, plasmapheresis, or treatment of post rituximab patients may be considered. Some of these types of preconditioning are standard of care for this autoimmune population and therefore are already considered to have a beneficial risk profile in this patient population. These other preconditioning regimens may cause serious adverse events, including hypotension, thromboembolism, and opportunistic infections.

We initiated our DesCAARTes ™ trial without a preconditioning regimen. If clinical data suggest that a preconditioning regimen is advisable, or if FDA requires that we employ a preconditioning regimen, we may employ such a regimen. If we ultimately use a preconditioning regimen, with or without lymphodepleting agents, prior to infusing patients with our CAAR T cell product candidates, our clinical patients may experience increased or more severe adverse effects specifically related to the preconditioning regimen, some of which may result in death. These undesirable side effects, whether associated with the preconditioning regimen alone or in combination with our CAAR T cell product candidates, could cause delays in patient enrollment in our clinical trials, could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a change to our clinical trial design, a more restrictive label or the delay or denial of regulatory approval by the FDA. Any of the foregoing may increase the duration and expense of the clinical development of our product candidates or limit market acceptance of such product candidates, if approved, any of which could have a material adverse effect on our business and financial condition. Even if we do not use a preconditioning regimen, patients may experience adverse effects related to our CAAR T cell product candidates, and our decision to design our clinical trials without preconditioning does not eliminate the risk of those side effects.

Our business is highly dependent on the success of our initial product candidates targeting B cell-mediated autoimmune diseases, particularly DSG3-CAART and MuSK-CAART. All of our product candidates will require significant additional preclinical and/or clinical development before we can seek regulatory approval for and launch a product commercially.

Our business and future success depend on our ability to obtain regulatory approval of, and then successfully launch and commercialize our initial product candidates targeting B cell-mediated autoimmune diseases, including DSG3-CAART, MuSK-CAART, DSG3/1-CAART, PLA2R-CAART and others that may be selected from preclinical programs. Our product candidates are in the early stages of development and will require additional preclinical studies, clinical trials, regulatory review and licensure, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. There is no guarantee that we will be able to advance our product candidates through clinical development or obtain marketing approval for any of our product candidates. The process for obtaining marketing approval for any product candidate is very long and risky and there will be significant challenges for us to address in order to obtain marketing approval as planned, if at all.

However, the initial clinical results we have observed may not be predictive of results of subsequent cohorts in this clinical trial, or of any future clinical trials. Because DSG3-CAART and MuSK-CAART are the first and second product candidates that we are testing in the clinic, we may experience preliminary complications surrounding trial design, protocol establishment and execution, establishing trial protocols, patient recruitment and enrollment, quality and supply of clinical doses, or safety issues. For example, while the majority of oncology CAR T clinical trials have been conducted with a lymphodepleting or other preconditioning regimen prior to infusion, we have not used pre-infusion lymphodepletion or other preconditioning regimen initially in our Phase 1 trial. However, we may determine that use of a lymphodepleting or other preconditioning regimen is necessary for our product candidates to be successful, which could result in delays in clinical development and will expose patients to the associated risks.

Additionally, a failure of our clinical trials of DSG3-CAART or MuSK-CAART could influence physicians' and regulators' opinions with regard to the viability of our CABA™ platform more broadly, particularly if treatment-related side effects are observed. The occurrence of any of these risks could significantly harm our development plans and business prospects. If treatment-related side effects are observed with the administration of DSG3-CAART or MuSK-CAART, or if they are viewed as less safe, potent or pure than other therapies, our ability to develop other CAAR T cell therapies may be significantly harmed.

We have never successfully completed any clinical trials, and we may be unable to do so for any product candidates we develop.

We have not yet demonstrated our ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Although our key employees have significant experience in leading clinical development programs, our experience conducting clinical trials with our product candidates is limited. We may not be able to file INDs for any of our other product candidates on the timelines we expect, if at all. For example, we cannot be certain that the IND-enabling studies for our future product candidates will be completed in a timely manner or be successful or that the manufacturing process will be validated in a timely manner. Even if we submit an IND for a future product candidate, the FDA may not clear the IND and allow us to begin clinical trials in a timely manner or at all. The timing of submissions on future product candidates will be dependent on further preclinical and manufacturing success. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing further clinical trials to begin, or that, once begun, issues will not arise that require us to suspend or terminate clinical trials. Commencing each of these clinical trials is subject to finalizing the trial design based on discussions with the FDA and other regulatory authorities. Any guidance we receive from the FDA or other regulatory authorities is subject to change. These regulatory authorities could change their position, including, on the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete additional clinical trials or impose stricter approval conditions than we currently expect.

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 modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- be subject to post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Risks Related to the Current Novel Coronavirus (COVID-19) Pandemic

The ongoing COVID-19 pandemic and the future outbreak of other highly infectious or contagious diseases could seriously harm our research, development and potential future commercialization efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.

Public health crises such as pandemics or similar outbreaks could adversely impact our business, the business operations of third parties on whom we rely and our ongoing or planned research and development activities. While progress has been made in the fight against the ongoing COVID-19 pandemic, including the broad dissemination and administration of vaccines in certain countries, the COVID-19 pandemic has continued spread globally, including in all 50 states within the United States, including Philadelphia, Pennsylvania where our primary office and laboratory space, as well as certain of our CMO partners, are located. The COVID-19 pandemic has continued to evolve as new variants of COVID-19 have been identified and spread, which have led to various responses, including government-imposed quarantines, travel restrictions and other public health safety measures in response to the emergence of new variants. The extent to which COVID-19 will continue to impact our operations or those of our third party partners will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the pandemic, new information that may emerge concerning the severity of COVID-19, the impact of new strains of the virus, the effectiveness, availability and utilization of vaccines and the actions to contain COVID-19 or treat its impact, among others. Further, since the beginning of the COVID-19 pandemic, three vaccines for COVID-19 have received Emergency Use Authorization by the FDA and two of those

later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials.

Additionally, timely enrollment in our ongoing and planned clinical trials is dependent upon clinical trial sites which may be adversely affected by global health matters, such as COVID-19. The ongoing COVID-19 pandemic could result in increased adverse events and deaths in our clinical trials due to COVID-19 related infections, and if we decide to implement a lymphodepleting preconditioning regimen, patients are likely to be more immunosuppressed and therefore at a greater risk of developing more severe symptoms from a COVID-19 infection. Some factors from the ongoing COVID-19 pandemic that have delayed and could further delay or otherwise adversely affect enrollment in the clinical trials of our product candidates, as well as our business generally, include:

- the potential diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our prospective clinical trials and the need for drugs, such as tocilizumab, and other supplies that clinical trial sites must have on hand to conduct our clinical trials to be used to treat COVID-19;
- limitations on travel that could interrupt key trial and business activities, such as clinical trial site initiations and monitoring, domestic and international travel by employees, contractors or patients to clinical trial sites, including any government-imposed travel restrictions or quarantines that will impact the ability or willingness of patients, employees or contractors to travel to our clinical trial sites or secure visas or entry permissions, a loss of face-to-face meetings and other interactions with potential partners, any of which could delay or adversely impact the conduct or progress of our prospective clinical trials;
- interruption in global shipping affecting the transport of clinical trial materials, such as patient samples, investigational drug product and conditioning drugs and other supplies used in our prospective clinical trials;
- interruptions in operations at our third-party manufacturers, which could result in delays or disruptions in the supply of our current product candidates and any future product candidates; and
- business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, product manufacturing and supply, staffing shortages, travel limitations or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees and other important agencies and contractors.

These and other factors arising from the ongoing COVID-19 pandemic could worsen. Any of these factors, and other factors related to any such disruptions that are unforeseen, could have a material adverse effect on our business and our results of operation and financial condition. Further, uncertainty around these and related issues could lead to adverse effects on the economy of the United States and other economies, which could impact our ability to raise the necessary capital needed to develop and commercialize our product candidates.

Risks Related to the Industry

Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.

Undesirable or unacceptable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA. Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of subjects and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the drug. Undesirable side effects could also result in an expansion in the size of our clinical trials, increasing the expected costs

and timeline of our clinical trials. Additionally, results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics.

Licensed CAR T cell therapies and those under development have shown frequent rates of CRS and neurotoxicity, and adverse events have resulted in the death of patients. Similar adverse events could occur during treatment with our CAAR T cell product candidates. For example, activation of CAAR T cells by patient autoantibodies or alloantibodies could stimulate CRS. When CAAR T cells are infused and the CAAR binds to soluble antibodies in the blood or tissues of treated patients, these soluble antibodies may cause the CAAR T cells to proliferate, resulting in an activation of the immune system that is too high, leading to CRS. Further, it is possible that patients will exhibit acute rejection of the CAAR T cells because of preexisting immunity to the antigen within the CAAR. This could render our product candidates ineffective.

If unacceptable toxicities or health risks, including risks inferred from other unrelated immunotherapy trials, arise in the development of our product candidates, we could suspend or terminate our trials or the FDA, the Data Safety Monitoring Board, or DSMB, or local regulatory authorities such as institutional review boards, or IRBs, could recommend or order us to cease clinical trials. Regulatory authorities, such as the FDA, could also 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 subjects to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from T cell therapy are not normally encountered in the general patient population and by medical personnel. We expect to have to train medical personnel using CAAR T cell product candidates to understand the side effect profile of our product candidates for both our preclinical studies and clinical trials and upon any commercialization of any of our product candidates, if licensed. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient deaths. Any of these occurrences may harm our business, financial condition and prospects significantly.

Our preclinical studies and clinical trials may fail to demonstrate the safety, potency and purity of any of our product candidates, which would prevent or delay regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are safe, potent and pure for use in each target indication. Clinical trials are expensive and can take many years to complete, and their outcomes are inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, including in any post-approval studies of our product candidates. In addition, initial success in any clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety, potency and purity profile despite having progressed through preclinical studies and initial clinical trials.

A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of potency or efficacy, insufficient durability of potency or efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical and other nonclinical findings made while clinical trials were underway, or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval. Most product candidates that commence clinical trials are never approved as products.

Any preclinical studies or clinical trials that we may conduct may not demonstrate the safety, potency and purity necessary to obtain regulatory approval to market our product candidates. If the results of our ongoing or future preclinical studies and clinical trials are inconclusive with respect to evaluations of efficacy, the safety, potency and purity of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for such product candidates. In some instances, there can be significant variability in evaluations of efficacy, safety, potency or purity results between different preclinical studies and clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. For example, because our CAAR T cell product candidates only target approximately 0.01% to 1% of the B cells in a patient, they may not engage enough of the target to achieve

adequate engraftment necessary for elimination of all pathogenic B cells. Insufficient safety or potency in clinical trials may delay product development to enable time to modify the product candidate for next generation approaches or make manufacturing changes or may lead us to discontinue development of the product candidate.

Additionally, our ongoing clinical trials utilize, and our planned trials may utilize, an "open-label" trial design. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an active drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

In addition, for DSG3-CAART, MuSK-CAART and any future trials that may be completed, we cannot guarantee that the FDA will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA to support a marketing application, approval of our product candidates may be significantly delayed, or we may be required to expend significant additional resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates.

Interim, topline or preliminary data from any preclinical studies or clinical trials that we conduct may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.

Our DesCAARTes™ trial and our planned MusCAARTes™ trial are both designed as open-label trials. From time to time, we may publicly disclose interim, preliminary or topline data from our preclinical studies and clinical trials, including safety data and evaluations of efficacy, which will be based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following our receipt of additional data or a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. For example, we have disclosed preliminary safety data from the first four cohorts of our DesCAARTes™ trial. We have also disclosed a dose dependent increase in persistence of DSG3-CAART observed in the third 500 million cell cohort relative to the first two low dose cohorts throughout the 28 days following infusion. Additionally, we disclosed top-line data on biologic activity from the first two low dose cohorts, and no clear evidence of biologic activity was observed. However, the trial is in its early stages and additional data from these initial cohorts, data from subsequent patients and data from patients at higher dosing levels may not be positive with respect to safety, target engagement or evidence of early signs of biologic activity.

As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from planned interim analyses in our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or our competitors, or by patients or caregivers who are aware that a patient is receiving investigational product, due to the open-label design of the trial, could result in volatility in the price of our common stock.

Regulatory agencies, including the FDA, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general.

If the interim, topline or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

The increasing use of social media platforms presents new risks and challenges.

Social media is increasingly being used to communicate about our clinical development programs and the diseases our product candidates are being developed to treat. We intend to utilize appropriate social media in connection with communicating about our development programs. Social media practices in the biopharmaceutical industry continue to evolve and regulations relating to such use are not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media channels to report an alleged adverse event during a clinical trial. When such disclosures occur, there is a risk that we fail to monitor and comply with applicable adverse event reporting obligations, or we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our investigational products. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website, or a risk that a post on a social networking website by any of our employees may be construed as inappropriate promotion. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions, or incur other harm to our business.

We may encounter substantial delays in our clinical trials or may not be able to conduct our trials on the timelines we expect or at all.

Clinical testing is expensive, time consuming and subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. Even if these trials begin as planned, issues may arise that could suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our ongoing and future clinical trials may not be successful. Events that may prevent successful or timely completion of clinical development include:

- inability to generate sufficient preclinical, toxicology or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- delays in developing suitable assays for screening patients for eligibility for clinical trials with respect to certain product candidates;
- delays in reaching a consensus with the FDA and other regulatory agencies on trial design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in obtaining required institutional review board, or IRB, approval at each clinical trial site;
- imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including after review of an IND submission or amendment, or equivalent application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; a negative finding from an inspection of our clinical study operations or study sites; developments on trials conducted by competitors for related technology that raises FDA concerns about risk to patients of the technology broadly; or if FDA finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- delays in recruiting eligible patients to participate in our clinical trials;
- delays in treating one or more patients, once enrolled, due to a patient's inability to accommodate parts of the complex study procedures schedule;

- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties or us to adhere to clinical trial requirements and the potential termination of ongoing agreements with our CROs;
- limitations on our recourse in our CRO relationship with Penn as compared to a CRO that is not an academic institution;
- failure to perform in accordance with the FDA's Good Clinical Practice, or GCP, requirements or applicable regulatory guidelines in other countries;
- transfer of manufacturing processes to any new CMO or our own manufacturing facilities or any other development or commercialization partner for the manufacture of product candidates;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- patients dropping out of a trial;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon product development programs;
- delays or failure to secure supply agreements with suitable raw material suppliers, or any failures by suppliers to meet our quantity or quality requirements for necessary raw materials; and
- delays in manufacturing or inability to manufacture sufficient clinical supply (for example, due to capacity constraints, supply interruption, or the need to engineer the process to meet higher dose requirements), testing, releasing, validating or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue. In December 2021, we disclosed our intent to implement an enhanced manufacturing process for our DSG3-CAART program, subject to an IND amendment. Our inability to effectively implement, or a delay in implementation of, such enhanced manufacturing process may prevent successful or timely completion of clinical development. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to, or we may elect to, conduct additional trials to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which our product candidates and products, if licensed, have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

We could also encounter delays if a clinical trial is suspended or terminated by us, the FDA or other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. 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.

Delays in the initiation, conduct or completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, 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. In the event we identify any additional product candidates to pursue, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin in a timely manner, if at all. Any of these occurrences may significantly harm our business, financial condition and prospects.

Monitoring safety of patients receiving our product candidates will be challenging, which could adversely affect our ability to obtain regulatory approval and commercialize our product candidates.

For our clinical trials of DSG3-CAART, MuSK-CAART and our other product candidates, we expect to continue to contract with Penn and other academic medical centers and hospitals experienced in the assessment and management of toxicities arising during clinical trials. In the future, we may also contract with non-academic medical centers and hospitals with similar capabilities. Nonetheless, these centers and hospitals may have difficulty observing patients, including due to failure by patients to comply with post-clinical trial follow-up programs, and treating toxicities, which may be more challenging due to personnel changes, inexperience, shift changes, house staff coverage or related issues. This could lead to more severe or prolonged toxicities or even patient deaths, which could result in us or the FDA delaying, suspending or terminating one or more of our clinical trials, and which could jeopardize regulatory approval. We also expect the centers using DSG3-CAART, MuSK-CAART and our other product candidates, if licensed, on a commercial basis could have similar difficulty in managing adverse events. Medicines used at centers to help manage adverse side effects of DSG3-CAART, MuSK-CAART and our other product candidates may not adequately control the side effects and/or may have a detrimental impact on the efficacy of the treatment.

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

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

- the size and nature of the patient population;
- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- recruiting an adequate number of suitable patients to participate in a clinical trial;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining IRB and other required reviewing body approval at each clinical trial site;
- the proximity of patients to trial sites;
- the design of the trial and whether the FDA agrees to the design and implementation of the trial;
- our ability to identify clinical trial sites and recruit clinical trial investigators with the appropriate capabilities, competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;

- the occurrence of dose-limiting toxicity in the clinical trial;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will drop out of the trials before the infusion of our product candidates or trial completion; and
- the ability of patients to meet the complex follow-up requirements of the clinical trial.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, some of our clinical trial sites may also be used by some of our competitors, which may reduce the number of patients who are available for our clinical trials in that clinical trial site.

Moreover, because our product candidates represent a departure from more commonly used methods for B cell-mediated autoimmune disease treatment, potential patients and their doctors may be inclined to use conventional therapies, such as corticosteroids or systemic immunosuppressive medications, rather than enroll patients in our clinical trial.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our ongoing and planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

Our DesCAARTes™ trial, our planned MusCAARTes™ trial and any additional expected Phase 1 clinical trials for each of our product candidates will be pilot dose escalation studies with a limited number of patients. The activity and toxicity data from these clinical trials of our product candidates may differ from future results of Phase 2 and/or Phase 3 clinical trials that enroll a larger number of patients.

Since the number of patients that we plan to dose in our DesCAARTes™ trial and our planned MusCAARTes™ trial is small, the results from such clinical trials, once completed, may be less reliable than results achieved in larger clinical trials, which may hinder our efforts to obtain regulatory approval for our product candidates. In both our DesCAARTes™ trial and our planned MusCAARTes™ trial, we plan to evaluate the toxicity profile of our product candidates and establish the recommended dose for the next clinical trial. The preliminary results of clinical trials with smaller sample sizes, such as our DesCAARTes™ trial and our planned MusCAARTes™ trial, can be disproportionately influenced by various biases associated with the conduct of small clinical trials, such as the potential failure of the smaller sample size to accurately depict the features of the broader patient population, which limits the ability to generalize the results across a broader community, thus making the clinical trial results less reliable than clinical trials with a larger number of patients. As a result, there may be less certainty that such product candidates would achieve a statistically significant effect in any future clinical trials. If we conduct any future clinical trials of DSG3-CAART or MuSK-CAART, we may not achieve a statistically significant result or the same level of statistical significance, if any, that we might have anticipated based on the results observed in our DesCAARTes™ trial and our planned MusCAARTes™ trial, respectively.

Risks Related to Sales, Marketing and Competition

The market opportunities for our product candidates may be limited to those patients who are ineligible for or have failed prior treatments and may be small.

Our projections of both the number of people who have the B cell-mediated autoimmune diseases we are targeting, as well as the subset of people with these diseases in a position to receive second or later lines of 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, or market research and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these B cell-mediated autoimmune diseases. 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 expect our lead product candidate, DSG3-CAART, to initially target a small patient population that suffers from mPV. Furthermore, in the event we use a preconditioning regimen for any of our CAAR T cell product candidates, then patients for whom the preconditioning regimen is contraindicated, or is not acceptable to the patient, may not be eligible for treatment with the product candidate, further reducing the potential target population. 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.

We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

The biopharmaceutical and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong focus on intellectual property. We face competition from many different players, including large and specialty pharmaceutical and biotechnology companies, academic research organizations and governmental agencies. Any therapeutic candidates we successfully develop and commercialize will compete with the existing standard of care as well as novel therapies that may gain regulatory approval in the future. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well-established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. We believe we are the first and only company developing CAAR T drug candidates for the treatment of B cell-mediated autoimmune diseases. However, despite the significant differences in discovery, development and target populations between oncology and autoimmune targets, we recognize that companies with an investment and expertise in CAR T cell development for oncology indications could attempt to leverage their expertise into B cell-mediated autoimmune disease affected populations. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products.

Specifically, while rituximab is the first drug for the treatment of PV, the target indication of our lead product candidate, DSG3-CAART, to have received regulatory approval in the United States in over 60 years, we are aware that multiple biopharmaceutical companies have therapies in clinical development. We are also aware of other biopharmaceutical companies developing therapies for muscle-specific kinase myasthenia gravis, or MuSK MG, PLA2R-associated membranous nephropathy, or PLA2R MN, and Hemophilia A patients who develop alloantibodies against FVIII. While we do not expect these product candidates to be directly competitive to our product candidates, even if we obtain regulatory approval of our product candidates, the availability and price of these other products could limit the demand and the price we are able to charge for our product candidates. We may not be able to implement our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug or biologic products or choose to reserve our product candidates for use in limited circumstances.

Even if we obtain regulatory approval of our product candidates, the products may not gain the market acceptance among physicians, patients, hospitals, treatment centers and others in the medical community necessary for commercial success.

The use of engineered T cells as a potential treatment for B cell-mediated autoimmune diseases is a recent development and may not become broadly accepted by physicians, patients, hospitals, treatment centers and others in the medical community. We expect physicians to be particularly influential and we may not be able to convince them to use our product candidates for many reasons. Additional factors will influence whether our product candidates are accepted in the market, including:

- the clinical indications for which our product candidates are licensed;
- physicians, hospitals, treatment centers and patients considering our product candidates as a safe and effective treatment;
- the potential and perceived advantages of our product candidates over alternative treatments;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA;
- the timing of market introduction of our product candidates as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement and pricing by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage and adequate reimbursement by third-party payors and government authorities;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies; and
- the effectiveness of our sales and marketing efforts.

The product candidates we plan to develop and commercialize are premised on offering a potential cure for B cell-mediated autoimmune diseases, which may result in a high degree of uncertainty related to pricing and long-term demand for our product. Our target patient populations are relatively small. Because of this pricing and demand for our product candidates, if licensed, may not be adequate to support an extended period of commercial viability, which could adversely affect our continued ability to successfully produce and market our product or any follow-on products.

In addition, if our product candidates are licensed but fail to achieve market acceptance among physicians, patients, hospitals, treatment centers or others in the medical community, we will not be able to generate significant revenue. Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete.

Risks Related to Business Development

We may not be successful in our efforts to identify additional product candidates. Due to our limited resources and access to capital, we must prioritize development of certain product candidates, which may prove to be wrong and may adversely affect our business.

Although we intend to explore other therapeutic opportunities, in addition to the product candidates that we are currently developing, we may fail to identify viable new product candidates for clinical development for a number of reasons. If we fail to identify additional potential product candidates, our business could be materially harmed.

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

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

Because we have limited financial and human resources, we intend to initially focus on research programs and product candidates for a limited set of indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential product candidates or other potential programs that ultimately prove to be unsuccessful.

If we fail to develop additional product candidates, our commercial opportunity will be limited.

One of our core strategies is to pursue clinical development of additional product candidates beyond DSG3-CAART, MuSK-CAART, DSG3/1-CAART, FVIII-CAART and PLA2R-CAART. Developing, obtaining regulatory approval and commercializing additional CAAR T cell product candidates will require substantial additional funding and is prone to the risks of failure inherent in medical product development. We cannot provide you any assurance that we will be able to successfully advance any of these additional product candidates through the development process.

Even if we receive FDA approval to market additional product candidates for the treatment of B cell-mediated autoimmune diseases, we cannot assure you that any such product candidates will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. If we are unable to successfully develop and commercialize additional product candidates, our commercial opportunity will be limited. Moreover, a failure in obtaining regulatory approval of additional product candidates may have a negative effect on the approval process of any other, or result in losing approval of any approved, product candidate.

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

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific, and medical personnel, including our Chief Executive Officer and President, our Scientific Advisory Board members, our President, Science and Technology, our Chief Medical Officer, and our Chief Financial Officer. The loss of the services of any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements could result in delays in product development and harm our business.

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

We expect to grow the size of our organization, and we may experience difficulties in managing this growth.

As of December 31, 2021, we had 53 full-time employees and one part-time employee. As our development and commercialization plans and strategies develop, and as we continue to transition into operating as a public company, we expect to rapidly expand our employee base and continue to add managerial, operational, sales, research and development, marketing, financial and other personnel. For example, we are still dependent on Penn and certain Penn-affiliated entities to continue providing certain research and development as well as manufacturing services under that certain research services agreement. Current and future growth imposes significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, retaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

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

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including certain research and development as well as general and administrative support, pursuant to agreements which expire after a certain period of time. There can be no assurance that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, or if we are not able to raise sufficient funds in the future to support our hiring efforts beyond our research and development personnel, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, Penn's operations and those of any CMOs, CROs and other contractors and consultants that we may engage could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We currently rely on Penn to produce and process our first product candidate and anticipate that in the future we will rely on a third-party CMO for the same. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

In addition, due to the ongoing COVID-19 pandemic, our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business operations. Further, 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 other important agencies and contractors.

Risks Related to Litigation

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

We face an inherent risk of product liability as a result of the 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 our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical 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 or a breach of warranties. 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:

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

Since we have not yet commenced marketing of any products, we do not yet hold product liability insurance for commercialization of our product candidates. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with corporate collaborators. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. Assuming we obtained clinical

trial insurance for our clinical trials, we may have to pay amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Risks Related to Our Financial Condition and Capital Requirements

Risks Related to Past Financial Condition

We have incurred net losses in every period since our inception and anticipate that we will incur substantial net losses over the next several years, and may never achieve or maintain profitability.

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 effect or an acceptable safety profile, gain regulatory approval and become commercially viable. We initially licensed rights to the patents underlying our product candidates in August 2018 and initiated our DesCAARTes™ trial in June 2020. We have no products licensed for commercial sale, and we will continue to incur significant research and development and other expenses related to our ongoing operations. Our net losses may fluctuate significantly from quarter to quarter and year to year. We have to date financed our operations primarily through private placements of our preferred stock, the sale of common stock in our initial public offering and sales of our common stock from time to time in "at-the-market" offerings.

As a result, we are not profitable and have incurred net losses in each period since our inception. For the years ended December 31, 2021 and 2020, we recorded net losses of $46.3 million and $33.3 million, respectively. As of December 31, 2021, we had an accumulated deficit of $112.6 million. We expect to incur significant losses for the foreseeable future, and we expect these losses to increase substantially if, and as, we:

- continue our research and development efforts and submit additional INDs for our product candidates;
- conduct preclinical studies and clinical trials for our current and future product candidates;
- further develop our product candidate platform;
- continue to discover and develop additional product candidates;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, scientific manufacturing and commercial personnel;
- establish a commercial manufacturing source and secure supply chain capacity sufficient to provide commercial quantities of any product candidates for which we may obtain regulatory approval, whether through a CMO or through a manufacturing facility that we establish;
- acquire or in-license other product candidates and technologies, including advanced manufacturing and translational capabilities that we will need for the further development and possible commercialization of our product candidates;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to support the sales and marketing of any product candidates for which we may obtain marketing approvals; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, as well as to support our transition to a public company.

To become and remain profitable, we must succeed in developing, and eventually commercializing, a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the

preliminary stages of most of these activities and have not yet demonstrated our ability to successfully develop any product candidate, obtain regulatory approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. We may never be able to develop, manufacture or commercialize a marketable product.

Even if we are able to succeed in these activities, we may never generate revenues that are significant enough to achieve profitability. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses will increase if, among other things:

- there are any delays in completing our clinical trials or the development of any of our product candidates;
- we are required by the FDA or other regulatory authorities to perform trials or studies in addition to, or different than, those expected; or
- there are any third-party challenges to our intellectual property or we need to defend against any intellectual property-related claim.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, if ever, we will be able to achieve profitability. Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop, seek regulatory approval for and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We have a limited operating history, which may make it difficult to evaluate the success of our business to date and to assess our future viability, and we may face significant challenges and expense as we test our product candidates and build our capabilities.

We were incorporated in 2017 and initially acquired rights to license certain patent rights Penn in August 2018. We are early in our development efforts, have a limited operating history and are subject to the risks inherent to any newly-formed organization, including, among others, risks that we may not be able to hire sufficient qualified personnel and establish operating controls and procedures.

Our limited operating history, particularly in light of the rapidly evolving cell therapy field, may make it difficult to evaluate our technology and industry and predict our future performance. Our short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer. Similarly, we expect that our financial condition and operating results will fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. As a result, our shareholders should not rely upon the results of any quarterly or annual period as an indicator of future operating performance.

We currently do not have in-house resources sufficient to enable the development of our product candidates, including our CAAR T cell platform. We are reliant on several manufacturing and support services from Penn through a Master Translational Research Services Agreement, or the Services Agreement, as well as certain research and development and general and administrative services through three sponsored research agreements. We also rely on Penn for access to key technologies for current manufacturing of our product candidates. As we build our own capabilities, and enter into agreements with third parties, we expect to encounter risks and uncertainties frequently experienced by growing companies in new and rapidly evolving fields, including the risks and uncertainties described herein. Our ability to rely on services from Penn is limited to a specified period of time, to specific capabilities, and is subject to Penn's right to terminate these services with or without cause. If we are unable to establish necessary relationships with third party partners and build our own capabilities, our operating and financial results could differ materially from our expectations, and our business could suffer.

All of our programs require additional preclinical research and development, clinical development, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, capacity and expertise, building of a commercial

organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. Other programs of ours require additional discovery research and then preclinical and clinical development. In addition, our product candidates must be licensed for marketing by the FDA before we may commercialize any product.

In addition, as an early-stage company, we have encountered and may continue to encounter unforeseen expenses, difficulties, complications, delays and other known and unknown circumstances. As we advance our product candidates, we will need to transition from a company with a research focus to a company capable of supporting clinical development and if successful, commercial activities. We may not be successful in such a transition.

We have not generated any revenue from our product candidates and our ability to generate revenue from product sales and become profitable depends significantly on our success in a number of areas.

To become and remain profitable, we or any potential future collaborator must develop and eventually commercialize products with significant market potential at an adequate profit margin after cost of goods sold and other expenses. All of our product candidates are in the early stages of development and we will require additional preclinical studies, clinical development, regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. We initiated our DesCAARTes ™ trial of DSG3-CAART, our most advanced product candidate, targeting pathogenic B cells in patients with mucosal pemphigus vulgaris, or mPV, in June 2020. Our IND for MuSK-CAART, targeting pathogenic B cells in a subset of patients with myasthenia gravis, or MG, became effective in January 2022. Our other product candidates, which include DSG3/1-CAART, targeting pathogenic B cells in patients with mucocutaneous pemphigus vulgaris, or mcPV, FVIII-CAART, for potential use as an adjunctive therapy targeting a subset of patients with Hemophilia A who develop alloantibody resistance to Factor VIII, or FVIII, replacement therapy, and PLA2R-CAART, targeting pathogenic B cells in patients with PLA2R-associated membranous nephropathy, or PLA2R-associated MN, have yet to complete IND-enabling studies. We have not yet administered any of our product candidates other than DSG3-CAART in humans and, as such, we face significant translational risk as our product candidates advance to the clinical stage. Our ability to generate revenue depends on a number of factors, including, but not limited to:

- 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 academic and commercial contractors;
- our ability to complete IND-enabling studies and successfully submit INDs or comparable applications;
- whether we are required by the FDA to conduct additional clinical trials or other studies beyond those planned to support the licensure and commercialization of our product candidates or any future product candidates;
- our ability to demonstrate to the satisfaction of the FDA the safety, potency, purity and acceptable risk to benefit profile of our product candidates or any future product candidates;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates or future product candidates, if any;
- the cost of manufacturing and processing our product candidates being greater than we anticipate;
- the timely receipt of necessary marketing approvals from the FDA;
- the willingness of physicians, operators of clinics and patients to utilize or adopt any of our product candidates or future product candidates to treat B cell-mediated autoimmune diseases;
- our ability and the ability of third parties with whom we contract to manufacture adequate clinical and commercial supplies of our product candidates or any future product candidates, remain in good standing with regulatory authorities and develop, validate and maintain commercially viable manufacturing processes that are compliant with FDA's current Good Manufacturing Practices, or cGMP;

- our ability to successfully develop a commercial and competitive strategy and thereafter commercialize our product candidates or any future product candidates in the United States, if licensed for marketing, reimbursement, sale and distribution, whether alone or in collaboration with others;
- patient demand for our product candidates and any future product candidates, if licensed; and
- our ability to establish and enforce intellectual property rights in and to our product candidates or any future product candidates.

Many of the factors listed above are beyond our control and could cause us to experience significant delays or prevent us from obtaining regulatory approvals or commercialize our product candidates. Even if we are able to commercialize our product candidates, we may not achieve profitability soon after generating product sales, if ever. If we are unable to generate sufficient revenue through the sale of our product candidates or any future product candidates, we may be unable to continue operations without continued funding.

If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Additionally, even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to research, develop and market additional product candidates. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Risks Related to Future Financial Condition

We will require substantial additional financing to develop and commercialize our product candidates and implement our operating plans. If we fail to obtain additional financing or cannot obtain financing at the levels we require due to we may be delayed in our plans or unable to complete the development and commercialization of our product candidates.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to continue the preclinical and clinical development of our product candidates, including our DesCAARTes™ trial, our planned MusCAARTes™ trial, and our research and development, preclinical studies and clinical trials for PLA2R-CAART, DSG3/1-CAART and FVIII-CAART and any future product candidates, to seek regulatory approvals for our product candidates, to enable commercial production of our products, if licensed, and to initiate and complete registration trials for multiple products. While we currently expect our existing cash and cash equivalents and investments to be sufficient to fund our operations through completion of Part A Dose Escalation of our DesCAARTes ™ trial, we expect to require significant additional financing to complete this Phase 1 trial, and any future clinical trials of DSG3-CAART and our other product candidates. Further, if licensed, we will require significant additional amounts of cash to launch and commercialize our product candidates.

As of December 31, 2021, we had $122.2 million of cash and cash equivalents and investments. On October 29, 2019, we completed an initial public offering of our common stock by issuing 7,275,501 shares of our common stock (including 475,501 shares of our common stock pursuant to the underwriters' option to purchase additional shares that we issued in November 2019), at $11.00 per share, for gross proceeds of $80.0 million, or net proceeds of $71.0 million. In 2021, we raised $49.7 million, or net proceeds of $48.3 million, in "at-the-market" offerings, pursuant to a Sales Agreement with Cowen and Company, LLC which provides for the offering, issuance and sale of up to an aggregate amount of $75.0 million of our common stock. Based on our current operating plan, we believe that our existing cash and cash equivalents and investments will be sufficient to fund our operations through the third quarter of 2023. However, we have based this estimate on assumptions that may prove to be wrong. Additionally, changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may require substantial additional capital for the further development and commercialization of our product candidates, including funding our internal manufacturing capabilities, and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate. Because the length of time and activities associated with development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. Our future funding requirements, both near- and long-term, will depend on many factors, including, but not limited to:

- the initiation, progress, timing, costs and results of preclinical studies and clinical trials for our product candidates;
- the clinical development plans we establish for these product candidates;
- the number and characteristics of product candidates that we may develop or in-license;
- the terms of any collaboration agreements we may choose to conclude;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates;
- the effect of competing technological and market developments;
- the costs of establishing and maintaining a supply chain for the development and manufacture of our product candidates;
- the cost and timing of establishing, expanding and scaling manufacturing capabilities;
- the cost of maintaining the amount patient data for which we would be responsible following commercialization of one or more of our product candidates; and
- the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own.

We cannot be certain that additional funding will be available on acceptable terms, or at all. As widely reported, global credit and financial markets have experienced extreme volatility and disruptions from the ongoing COVID-19 pandemic and related factors, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Until we are able to generate sufficient revenue to finance our cash requirements, we will need to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements. 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 our research and development initiatives and clinical development plans. We could be required to seek collaborators for our product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to our product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital may be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities and costs associated with operating a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to the holders of our common stock.

Pursuant to our equity incentive plans, our management is authorized to grant stock options to our employees, directors and consultants. Additionally, the number of shares of our common stock reserved for issuance under the 2019 Stock Option and Incentive Plan automatically increased on January 1, 2022 and will automatically increase each January 1 thereafter through and including January 1, 2029, by 4% of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by our board of directors. Unless our board of directors elects not to increase the number of shares available for future grant each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Risks Related to Our Intellectual Property

We rely heavily on certain in-licensed patent and other intellectual property rights in connection with our development of our product candidates and, if we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, we could lose license rights that are important to our business.

Our ability to develop and commercialize our product candidates is heavily dependent on in-licenses to patent rights and other intellectual property granted to us by third parties. For example, we depend heavily on our License Agreement with Penn and CHOP, which was entered into in 2018, amended and restated in July 2019, and further amended in May 2020 and October 2021, pursuant to which we obtained (a) a non-exclusive, non-sublicensable, worldwide research license to intellectual property controlled by Penn and CHOP to make, have made and use products in two subfields of use, (b) effective as of October 2018, an exclusive, worldwide, royalty-bearing license, with the right to sublicense, under certain of such intellectual property to make, use, sell, offer for sale and import products in the same two subfields of use, and (c) effective as of October 2018, a non-exclusive, worldwide, royalty-bearing license, with limited rights to sublicense, under certain of Penn's know-how, which know-how satisfies certain criteria and is listed on a mutually agreed to schedule, to make, have made, use, sell, offer for sale, import and have imported products in the same two subfields of use. We may enter into additional license agreements in the future. Our license agreement with Penn and CHOP imposes, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under these licenses, our licensors, including Penn and CHOP, may have the right to terminate these license agreements, in which event we might not be able to market our product candidates. Termination of any of our license agreements or reduction or elimination of our licensed rights may also result in our having to negotiate new or reinstated licenses with less favorable terms.

We may need to obtain additional licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current product candidates or future products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

Furthermore, in many cases, 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 in-license from third parties. For example, pursuant to our License Agreement with Penn and CHOP, Penn controls such activities for the patent rights licensed to us under such agreement. Therefore, although we provide input to Penn and CHOP on these activities, we cannot be certain that these patents will be prosecuted, maintained and enforced in a manner consistent with the best interests of our business. If our current or future licensors or collaboration partners fail to obtain, maintain or protect any patents or patent applications licensed to us, our rights to such patents and patent applications may be reduced or eliminated and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected.

Disputes may arise between us and our current and future licensors regarding intellectual property subject to a license agreement, including those related to:

- the scope of rights granted under the License Agreement and other interpretation-related issues;
- whether we have breached the License Agreement and whether any such breach is subject to a cure period;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and

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

Furthermore, disputes may arise between us and our current or future licensors regarding the ownership of intellectual property developed by us, such that we may be required to assign or otherwise transfer such intellectual property to such licensor. In the event that the assigned or transferred intellectual property is covered by an existing license agreement with such licensor we may be required to make additional royalty or milestone payments, or both, to such licensor. If the assigned or transferred intellectual property is not covered by an existing license agreement, then we may be required to enter into an additional license agreement to advance our research or allow commercialization of our product candidates, which may not be available on commercially reasonable terms or at all.

If disputes over intellectual property that we have licensed, or license in the future, prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

If our efforts to protect the proprietary nature of the intellectual property related to our current and any future product candidates are not adequate, we may not be able to compete effectively in our market.

Our success depends in large part on our ability to obtain and maintain intellectual property protection in the United States and other countries with respect to our product candidates. If we do not adequately protect or enforce our intellectual property rights, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we have in-licensed patent rights in the United States and abroad relating to the product candidates that are important to our business. The patent application and approval process is expensive, complex and time-consuming. Our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to biological and pharmaceutical products commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that our licensors were the first to make the inventions claimed in the patents or pending patent applications we in-license, or that our licensors were the first to file for patent protection of such inventions.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, the patents or pending patent applications we in-license may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in post-grant review procedures, derivation proceedings, reexaminations, or *inter partes* review in the United States, or oppositions and other comparable proceedings in foreign jurisdictions, challenging our patent rights or the patent rights of others. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of the patents we in-license or narrow the scope of our patent protection. In addition, the laws

of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, European patent law is more restrictive than U.S. patent law in connection with the patentability of methods of treatment of the human body.

We cannot predict whether the patent applications we in-license currently being pursued will issue as patents, whether the claims of any patent that has or may issue will provide us with a competitive advantage or prevent competitors from designing around the claims to develop competing technologies in a non-infringing manner, or whether we or our licensors will be able to successfully pursue patent applications in the future relating to our current product candidates or future products and product candidates. Moreover, the patent application and approval process is expensive and time-consuming. We or our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Furthermore, we, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to seek additional patent protection.

It is possible that defects of form in the preparation or filing of patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If there are material defects in the form, preparation, prosecution or enforcement of the patents or patent applications we in-license, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

Even if the patent applications we in-license issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patent rights by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our product candidates. Alternatively, our competitors may seek to market generic versions of any approved products by submitting abbreviated BLAs to the FDA during which process they may claim that patents licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our intellectual property rights, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find the patents we in-license invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have in-licensed valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

In the future, we likely will need to expand our patent portfolio to pursue patent coverage for new product candidates that we wish to develop. The patent prosecution process is competitive, and other companies, some which may have greater resources than we do in this area, may also be pursuing intellectual property rights that we may consider necessary or attractive in order to develop and commercialize future product candidates.

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

Filing, prosecuting, maintaining, defending and enforcing patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. The deadline to pursue protection in foreign jurisdictions for some of the patent families licensed under the License Agreement with Penn has not yet expired. Prior to applicable deadlines, we and Penn will need to decide where to pursue protection, and we will not have the opportunity to pursue protection unless we do so in applicable jurisdictions prior to the deadlines. Although our License Agreement grants us worldwide rights, there can be no assurance that we will obtain or maintain patent rights in or outside the United States under any future license agreements. 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 even in jurisdictions where we and our licensors pursue patent protection. Consequently, we and our licensors may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we and our licensors pursue patent protection, 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 and our licensors have not pursued and obtained patent protection to develop their own products and, further, may

export otherwise infringing products to territories where we and our licensors have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates and the patents we in-license or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of the patents we in-license or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights, even if obtained, in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put the patents we in-license at risk of being invalidated or interpreted narrowly and the patent applications we in-license 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.

We or our licensors may be subject to claims challenging the inventorship or ownership of the patents and other intellectual property that we own or license.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an ownership interest in the patents and intellectual property that we in-license or that we may own or in-license in the future. While it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own or such assignments may not be self-executing or may be breached. Our licensors may face similar obstacles. We or our licensors could be subject to ownership disputes arising, for example, from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. For example, our scientific co-founders, Drs. Payne and Milone, are members of our scientific advisory board and are also employed by and subject to Penn's intellectual property policy. Litigation may be necessary to defend against any claims challenging inventorship or ownership. If we or our licensors fail in defending any such claims, we may have to pay monetary damages and may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property, which could adversely impact our business, results of operations and financial condition.

Some intellectual property which we have in-licensed was discovered through government funded programs and thus is subject to federal regulations such as "march-in" rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers.

Certain of the intellectual property rights we have licensed, including rights licensed to us by Penn relating to our DSG3-CAART and DSG3/1-CAART product candidates, was generated through the use of U.S. government funding and may therefore be subject to certain federal laws and regulations. As a result, the U.S. government has certain rights to intellectual property embodied in our DSG3-CAART and DSG3/1-CAART product candidates and may have rights in future product candidates pursuant to the Bayh-Dole Act of 1980. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as "march-in rights". The U.S. government also has the right to take title to these inventions if we, or the applicable licensor, such as Penn, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U.S. government requires that products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the

United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for product candidates covered by such intellectual property.

We may become involved in lawsuits to protect or enforce our patent rights or other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe, misappropriate or otherwise violate patents, trademarks, copyrights or other intellectual property that we own or in-license. To counter infringement, misappropriation or other unauthorized use, we may be required to file claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived violators could provoke these parties to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their intellectual property, in addition to counterclaims asserting that the patents we in-license are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent we in-license is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that the patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving the patents we in-license could limit our ability to assert the patent we in-license against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition.

Even if we establish infringement, misappropriation or another violation of our intellectual property rights, the court may decide not to grant an injunction against the offender and instead award only monetary damages, which may or may not be an adequate remedy. 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 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 shares. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings. Any of the foregoing may have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Changes in either the patent laws or the interpretation of the patent laws in the United States or other jurisdictions could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. When implemented, the Leahy-Smith Act included several significant changes to U.S. patent law that impacted how patent rights could be prosecuted, enforced and defended. In particular, the Leahy-Smith Act also included provisions that switched the United States from a "first-to-invent" system to a "first-to-file" system, allowed third-party submission of prior art to the USPTO during patent prosecution and set forth additional procedures to attack the validity of a patent by the USPTO administered post grant proceedings. Under a first-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO developed new regulations and procedures governing the administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. It remains unclear what impact, if any, the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of the patent applications we in-license and the enforcement or defense of the issued patents we in-license, all of which could have a material adverse effect on our business.

The patent positions of companies engaged in the development and commercialization of biologics are particularly uncertain. For example, the Supreme Court of the United States issued its decision in Association for Molecular Pathology v. Myriad Genetics, Inc., or Myriad, a case involving patent claims held by Myriad Genetics, Inc. relating to the breast cancer susceptibility genes BRCA1 and BRCA2. Myriad held that an isolated segment of naturally occurring DNA, such as the DNA constituting the BRCA1 and BRCA2 genes, is not patent-eligible subject matter, but that complementary DNA, which is an artificial construct that may be created from RNA transcripts of genes, may be patent-eligible. Thereafter, the USPTO issued a guidance memorandum instructing USPTO examiners on the ramifications of the Prometheus and Myriad rulings and apply the Myriad ruling to natural products and principles including all naturally occurring nucleic acids. Certain claims of our in-licensed patent applications contain, and any future patents we may obtain may contain, claims that relate to specific recombinant DNA sequences that are naturally occurring at least in part and, therefore, could be the subject of future challenges made by third parties.

We cannot assure you that our efforts to seek patent protection for one or more of our product candidates will not be negatively impacted by this Supreme Court decision, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact the Supreme Court's decisions in Myriad may have on the ability of life science companies to obtain or enforce patents relating to their products in the future. These decisions, the guidance issued by the USPTO and rulings in other cases or changes in USPTO guidance or procedures could have a material adverse effect on our existing patent rights and our ability to protect and enforce our intellectual property in the future.

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

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect certain proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce, and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach.

In addition, our trade secrets may otherwise become known or be independently discovered by competitors. Competitors and other third parties could infringe, misappropriate or otherwise violate our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If our trade secrets are not adequately protected or sufficient to provide an advantage over our competitors, our competitive position could be adversely affected, as could our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets.

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

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. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of the product's approval by the FDA, only one patent applicable to an approved drug is eligible for the extension, and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. In the future, if and when our product candidates receive FDA approval, we plan to apply for patent term extensions on patents covering those

product candidates in any jurisdiction where these are available. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to the patents we in-license, or may grant more limited extensions than we request. Moreover, we may not receive 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. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Certain of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. Our licensors may face similar risks, which could have an adverse impact on intellectual property that is licensed to us.

We may become subject to claims that we are infringing certain third-party patents or other third-party intellectual property rights, any of which may prevent or delay our development and commercialization efforts and have a material adverse effect on our business.

Our commercial success depends in part on avoiding infringing, misappropriating and otherwise violating the patents and other intellectual property and proprietary rights of third parties. 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, and administrative proceedings such as interferences, *inter partes* review and post grant review proceedings before the USPTO and opposition proceedings before foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned or controlled by third parties, including our competitors, exist in the fields in which we are pursuing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we or our licensors are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, methods of manufacture or methods for treatment relating to our product candidates and, because patent applications can take many years to issue, there may be currently pending third party patent applications which may later result in issued patents, in each case that our product candidates, their manufacture or use may infringe or be alleged to infringe. We may fail to identify potentially relevant patents or patent applications, incorrectly conclude that a patent is invalid or does not cover our activities, or incorrectly conclude that a patent application is unlikely to issue in a form of relevance to our activities.

Parties making patent infringement claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, including demonstrating non-infringement, invalidity or unenforceability of the respective patent rights in question, regardless of their merit, is time-consuming, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. For example, in order to successfully challenge the validity of any U.S. patent in federal court, we would need to overcome a presumption of validity. This is a high burden requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, and we can provide no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. We may not have sufficient resources to bring these actions to a successful conclusion. 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 shares.

In the event that a holder of any such patents seeks to enforce its patent rights against us with respect to one or more of our product candidates, and our defenses against the infringement of such patent rights are unsuccessful, we may be precluded from commercializing our product candidates, even if approved, without first obtaining a license to some or all of these patents, which may not be available on commercially reasonable terms or at all. Moreover, we may be required to pay significant fees and royalties to secure a license to the applicable patents. Such a license may only be non-exclusive, in which case our ability to stop others from using or commercializing technology and products similar or identical to ours may be limited. Furthermore, we could be liable for damages to the holder of these patents, which may be significant and could include treble damages if we are found to have willfully infringed such patents. In the event that a challenge to these patents were to be unsuccessful or we were to become subject to litigation or unable to obtain a license on commercially reasonable terms with respect to these patents, it could harm our business, financial condition, results of operations and prospects.

We are aware of third-party issued U.S. patents relating to the lentiviral vectors which may be used in the manufacture or use of our product candidates. If these patent rights were enforced against us, we believe that we have defenses against any such action, including that these patents would not be infringed by our product candidates and/or that these patents are not valid. However, if these patents were enforced against us and defenses to such enforcement were unsuccessful, unless we obtain a license to these patents, which may not be available on commercially reasonable terms, or at all, we could be liable for damages and precluded from commercializing any product candidates that were ultimately held to infringe these patents, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Even in the absence of a finding of infringement, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, or at all. In that event, we would be unable to further develop and commercialize our product candidates. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. Any of the foregoing could materially adversely affect our business, results of operations and financial condition.

Intellectual property rights do not necessarily address all potential threats.

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

- others may be able to make products that are similar to our product candidates or utilize similar cell therapy technology but that are not covered by the claims of our current or future patent portfolio;
- we, or our current or future licensors or collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license now or that we may license or own in the future;
- we, or our current or future licensors or collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our licensed intellectual property rights;
- it is possible that our current or future licensed patent applications will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties 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;
- the patents of others may harm our business;
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent application covering such intellectual property; and

- third-party patents may issue with claims covering our activities; we may have infringement liability exposure arising from such patents.

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

Risks Related to Our Reliance on Third Parties

We are reliant on a research services agreement with Penn for a significant portion of our nonclinical research and development activities and current manufacturing activities.

If Penn and its affiliated entities were to fail to perform their obligations in accordance with the terms of the Services Agreement or terminate the Services Agreement with little notice, we may have difficulty continuing our normal business operations and our business prospects, financial condition and results of operations could be harmed. In addition, the termination of our relationship with Penn and the Services Agreement and any delay in appointing or finding a suitable replacement provider, if one exists, could make it difficult for us to operate our business for that period. Moreover, we will be reliant on Penn to assist us with any necessary technology transfer. Any delays or inadequacies in such technology transfer, or disputes regarding the scope of such technology transfer, could delay our operations, including our clinical trials, require us to expend additional resources and otherwise have an adverse effect on our business.

Additionally, over time we will need to transition from receiving the services that Penn currently provides to performing such services internally. The Services Agreement is scheduled to expire on the later of October 19, 2021 or completion of all research and development projects, and unless the Services Agreement is amended, Penn will not be obligated to provide any further services under the Services Agreement after that time. We currently anticipate that research and development projects under the Services Agreement will continue through at least 2023. In addition, Penn has the right to terminate the Services Agreement in whole at any time with 90 days' notice and to terminate any research and development project being performed under the Services Agreement if the Penn service provider appointed to lead such project is unavailable and Penn is unavailable to find a replacement within 60 days for such service provider. Penn also has the right to terminate certain manufacturing services being performed under the Services Agreement with 180 days' written notice. From time to time, we may enter into further addenda to the Services Agreement that provide Penn with the right to terminate such addenda with limited notice periods. If we do not have adequate personnel and capabilities at the time that we assume responsibilities for such services, we may not be successful in effectively or efficiently transitioning these services from Penn, which could disrupt our business and have a material adverse effect on our financial condition and results of operations. Further, we will incur costs relating to establishing our own financial, administrative, information technology and other support functions as well as running and maintaining such functions on a going-forward basis. In addition, the process of establishing such functions may distract our management from focusing on business and strategic opportunities and could result in disruptions to our business. Even if we are able to successfully transition these services, they may be more expensive or less efficient than the services we are receiving from Penn during the transition period.

We currently, and will likely continue to, rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates.

We depend and will continue to depend upon third parties, including independent investigators and collaborators, such as universities, medical institutions, CROs and strategic partners, to conduct our preclinical studies and clinical trials under agreements with us. Specifically, we depend on clinical trial sites to enroll patients and conduct the DesCAARTes™ trial and planned MusCAARTes™ trial in a timely and appropriate manner. If our clinical trial sites do not conduct the trials on the timeline we expect or otherwise fail to support the trials, our clinical trial results could be significantly delayed, thereby adversely impacting our leadership position in the CAAR T industry and our ability to progress additional product candidates. Further, although we intend to transition our manufacturing needs to a CMO and eventually secure our own clinical manufacturing facility, we must currently rely on Penn to manufacture supplies and process our product candidates. As we open additional clinical trial sites, we expect to have to negotiate

budgets and contracts with CROs and study sites, which may result in delays to our development timelines and increased costs.

We will rely heavily on these third parties, including Penn, to conduct our discovery efforts and manufacturing, and as a result, will have limited control over pace at which these activities are carried out. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with FDA's GCPs which are regulations and guidelines enforced by the FDA for product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. We cannot provide assurance that, upon inspection, such regulatory authorities will not determine that some or all of our clinical trials do not fully comply with the GCP requirements. For any violations of laws and regulations during the conduct of our clinical trials, we could be subject to untitled and warning letters or enforcement action that may include civil penalties up to and including criminal prosecution. In addition, our clinical trials must be conducted with biologic product produced under cGMPs and will require a large number of test patients. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

As widely reported, global credit and financial markets have experienced extreme volatility and disruptions from the ongoing COVID-19 pandemic and related factors, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. In the event that one or more of our current or future service providers, manufacturers and other partners do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, due to the economic downturn or for any other reasons, then we may not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines. Our failure or the failure of these third parties to comply with applicable regulatory requirements or our stated protocols could also subject us to enforcement action. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our clinical trials will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our ongoing preclinical and clinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical studies or other drug development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with trial sites, or any CRO that we may use in the future, terminates, we may not be able to enter into arrangements with alternative trial sites or CROs or do so on commercially reasonable terms. Switching or adding third parties to conduct our clinical trials involves substantial cost and requires extensive management time and focus. In addition, there is often a natural transition period when a new third party commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. For example, in October 2021, one of our CROs that provides data management, biostatistics and pharmacovigilance data services for the DesCAARTes™ trial, provided us a 60-day notice of termination for convenience, and as a result in December 2021 we transitioned to a new provider of data management, biostatistics and pharmacovigilance data services. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

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

We intend to rely on third parties to manufacture our clinical product supplies, and we may have to rely on third parties to produce and process our product candidates, if licensed.

Although we may eventually secure our own clinical manufacturing facility for any late phase clinical development that we undertake, we currently rely on third parties, including Penn, to supply raw materials and other important components that are used to manufacture our product candidates and intend in the future to rely on CMOs. In the case of any manufacturing performed for us by third parties, the services performed for us risk being delayed because of the competing priorities that such parties have for utilization of their manufacturing resources and any capacity issues that thereby arise.

We do not yet have sufficient information to reliably estimate the cost of the manufacturing and processing of our product candidates in clinical quantity or commercial quantity, and the actual cost to manufacture and process our product candidates could ultimately materially and adversely affect the commercial viability of our product candidates. As a result, we may never be able to develop a commercially viable product.

In addition, our anticipated reliance on a limited number of third-party manufacturers exposes us to the following risks:

- We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA may have questions regarding any replacement contractor. This may require new testing and regulatory interactions. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA questions, if any.
- Our third-party manufacturers might be unable to timely formulate and manufacture our product or produce the quantity and quality required to meet our clinical and commercial needs, if any.
- Contract manufacturers may not be able to execute our manufacturing procedures appropriately.
- Any contract manufacturers that we engage may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our product candidates.
- Manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMP and other government regulations. We do not have control over third-party manufacturers' compliance with these regulations and standards.
- We may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our product candidates.
- Our third-party manufacturers could breach or terminate their agreement with us.

Furthermore, all of our contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks related to the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our contract manufacturers' facilities generally. If the FDA does not approve these facilities for the manufacture of our product candidates or if any agency withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would negatively impact our ability to develop, obtain regulatory approval for or market our product candidates, if licensed.

Our contract manufacturers would also be subject to the same risks we face in developing our own manufacturing capabilities, as described above. Each of these risks could delay our clinical trials, the approval, if any of our product candidates by the FDA or the commercialization of our product candidates or result in higher costs or deprive us of potential product revenue. In addition, we will rely on third parties to perform release tests on our product

candidates prior to delivery to patients. If these tests are not appropriately done and test data are not reliable, patients could be put at risk of serious harm.

For more information, see "Risk Factors—Risks Related to Manufacturing and Supply".

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

We may form or seek strategic alliances, create joint ventures or collaborations or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any future product candidates that we may develop. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety, potency and purity. Any delays in entering into new strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

If we license products or businesses, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. For instance, our License Agreement with Penn and CHOP requires significant research and development commitments that may not result in the development and commercialization of our product candidates, including DSG3-CAART and our other product candidates. We cannot be certain that, following a strategic transaction or license, we will achieve the results, revenue or specific net income that justifies such transaction.

We may not realize the benefits of acquired assets or other strategic transactions, including any transactions whereby we acquire or license manufacturing and other advanced technologies.

In August 2018, we entered into a License Agreement with Penn and CHOP which was amended and restated in July 2019, and further amended in May 2020 and October 2021, or the License Agreement, pursuant to which we were granted licenses to certain patent rights for the research and development of products, as well as an exclusive license under those same patent rights to make, use, sell and import such products, in the autoimmune disease and alloimmune response subfields, in each case, for the treatment of humans.

We actively evaluate various strategic transactions on an ongoing basis. We may acquire other businesses, products or technologies as well as pursue joint ventures or investments in complementary businesses. The success of our strategic transactions, including the License Agreement, and any future strategic transactions depends on the risks and uncertainties involved including:

- unanticipated liabilities related to acquired companies or joint ventures;
- difficulties integrating acquired personnel, technologies and operations into our existing business;
- retention of key employees;
- diversion of management time and focus from operating our business to management of strategic alliances or joint ventures or acquisition integration challenges;
- increases in our expenses and reductions in our cash available for operations and other uses;
- disruption in our relationships with collaborators or suppliers as a result of such a transaction; and
- possible write-offs or impairment charges relating to acquired businesses or joint ventures.

If any of these risks or uncertainties occur, we may not realize the anticipated benefit of any acquisition or strategic transaction. Additionally, foreign acquisitions and joint ventures are subject to additional risks, including those related to integration of operations across different cultures and languages, currency risks, potentially adverse tax consequences of overseas operations and the particular economic, political and regulatory risks associated with specific countries.

Future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of debt, contingent liabilities or amortization expenses or write-offs of goodwill, any of which could harm our financial condition.

Risks Related to Manufacturing and Supply

We currently rely upon Penn for our manufacturing needs, and we intend to rely on other third parties for our future manufacturing needs prior to establishing our own manufacturing facility.

We are currently reliant upon Penn for our cell product manufacturing for our lead product candidate, DSG3-CAART. We have entered into agreements with CMOs and initiated tech transfer activities to secure the manufacturing supply chain for current and future product candidates. We will need to develop relationships with suppliers, increase the scale of production and demonstrate comparability of the material produced at these facilities to the material that was previously produced. Transferring manufacturing processes and know-how is complex and involves review and incorporation of both documented and undocumented processes that may have evolved over time.

In addition, transferring production to different facilities may require utilization of new or different processes to meet the specific requirements of a given facility. We would expect additional comparability work will also need to be conducted to support the transfer of certain manufacturing processes and process improvements. We cannot be certain that all relevant know-how and data has been adequately incorporated into the manufacturing process until the completion of studies (and the related evaluations) intended to demonstrate the comparability of material previously produced with that generated by any CMO that we engage for our manufacturing needs. If we are not able to successfully transfer and produce comparable product candidates, our ability to further develop and manufacture our product candidates may be negatively impacted.

We plan to eventually establish our own manufacturing facility. While the addition of our own manufacturing facility would provide us with future flexibility within our manufacturing network, we still may need to identify additional CMOs for continued production of supply for some or all of our product candidates. Given the nature of our manufacturing processes, the number of CMOs who possess the requisite skill and capability to manufacture our CAAR T cell immunotherapy product candidates is limited.

Further, we may not be able to achieve clinical manufacturing and cell processing through Penn on a timely basis, on our own or at any future CMO. While our current manufacturing process is based off the validated process developed at Penn for CD19 CAR T, or CART19, we have limited experience as an organization in managing the CAAR T engineering process. Finally, because clinical manufacturing and cell processing is highly complex and patient donor material is inherently variable, we cannot be sure that the manufacturing processes employed by Penn, any CMO that we engage in the future, or by us at a manufacturing facility that we establish will consistently result in T cells that will be safe and effective.

Our product candidates are uniquely manufactured. If we, Penn or any of our third-party manufacturers encounter difficulties in manufacturing our product candidates, our ability to provide supply of our product candidates for clinical trials or, if licensed, for commercial sale, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

The manufacturing process used to produce our product candidates is complex and novel, and it has not yet been validated for commercial production. Among the complex processes used in the manufacture of our product candidates is the manufacture of the lentiviral delivery vector used to deliver the applicable CAAR gene into the T cells. For example, the manufacture of our product candidates includes harvesting white blood cells from each patient, stimulating certain T cells from the white blood cells and thereby causing them to activate and proliferate, combining

patient T cells with our lentiviral delivery vector through a process known as transduction, expanding the transduced T cells to obtain the desired dose, and ultimately infusing the modified T cells back into the patient's body. Notably, the manufacture of both DSG3/1-CAART and FVIII-CAART may be more challenging or require new gene delivery technology due to the need to deliver large transgenes for these programs, and vector delivery systems have size limitations. Because of these complexities, the cost to manufacture our product candidates is higher than traditional small molecule chemical compounds and monoclonal antibodies, and the manufacturing process is less reliable and is more difficult to reproduce. Furthermore, our manufacturing process development and scale-up is at an early stage. The actual cost to manufacture and process our product candidates could be greater than we expect and could materially and adversely affect the commercial viability of our product candidates.

Our manufacturing process may be susceptible to technical and logistics delays or failures due to the fact that each patient is an independent manufacturing lot, and also due to unique supply chain requirements. These include the collection of white blood cells from patients' blood, variability in the quality of white blood cells collected from patients' blood, cryopreservation of the white blood cells collected, packaging and shipment of frozen white blood cells to the manufacturing site in order to enable multi-site studies, procurement of lentiviral vectors that meet potency and purity requirements and shipment to the product candidate manufacturing site, shipment of the final product to clinical centers, manufacturing issues associated with interruptions in the manufacturing process, scheduling constraints for cell manufacturing slots, process contamination, equipment or reagent failure, improper installation or operation of equipment, vendor or operator error, and inconsistency in cell growth. Even minor deviations from normal manufacturing processes could result in reduced production yields, lot failures, product defects, product recalls, product liability claims and other supply disruptions. If microbial, viral, or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, production at such manufacturing facilities may be interrupted for an extended period of time to investigate and remedy the contamination. Further, as product candidates are developed through preclinical studies to late-stage clinical trials toward approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes may result in the need to enroll additional patients or to conduct additional clinical studies to evaluate the impact of changes on product safety and efficacy. Penn has informed us that it will be unable provide clinical supply for any late-phase clinical trials of our product candidates that we may conduct. Therefore, we will need to enter into new agreements with CMOs to produce clinical supply of our product candidates for late-phase clinical trials. We cannot guarantee that we will be able to enter into such agreements on commercially acceptable terms, if at all. We will need to transfer the technology to manufacture our product candidates to these CMOs, and these CMOs may decide or be required to adopt different manufacturing protocols or processes, which may require us to amend any ongoing or proposed clinical trial protocols or perform additional preclinical studies to demonstrate the comparability of any such new manufacturing protocols or processes. We cannot provide any assurance that Penn will provide adequate support to efficiently and effectively transfer the technology or that disputes will not arise between us and Penn regarding the necessary scope of technology transfer, that the technology transfer will be successful, or that any CMO will be successful in producing our product candidates in sufficient quantities or of acceptable quality, if at all. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of ongoing and planned clinical trials or other future clinical trials.

Although we continue to optimize our manufacturing process for our product candidates, doing so is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, lot consistency and timely availability of reagents and/or raw materials. We ultimately may not be successful in transferring our production system from our contract manufacturer to any manufacturing facilities we may establish ourselves, or our contract manufacturer may not have the necessary capabilities to complete the implementation and development process. If we are unable to adequately validate or scale-up the manufacturing process for our product candidates with our current manufacturer, we will need to transfer to another manufacturer and complete the manufacturing validation process, which can be lengthy. If we are able to adequately validate and scale-up the manufacturing process for our product candidates with a contract manufacturer, we will still need to negotiate with such contract manufacturer an agreement for commercial supply and it is not certain we will be able to come to agreement on terms acceptable to us. As a result, we may ultimately be unable to reduce the cost of goods for our product candidates to levels that will allow for an attractive return on investment if and when those product candidates are commercialized.

In addition, many of the components which are required to support our cell manufacturing process, such as equipment, media, growth factors and disposables, are highly specialized and it is possible that the supply chain for these materials may be interrupted. If we are unable to promptly remedy such interruption, then there may be delays to our clinical development efforts.

The manufacturing process for any products that we may develop is subject to the FDA approval process, and we will need to contract with manufacturers who can meet all applicable FDA requirements on an ongoing basis.

The manufacturing process for any products that we may develop is subject to the FDA approval process, and we will need to contract with manufacturers who can meet all applicable FDA requirements on an ongoing basis. If we or our CMOs are unable to reliably produce products to specifications acceptable to the FDA, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CMOs will be able to manufacture the approved product in accordance with requirements from the FDA, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, suspension of production or recalls of the product candidates or marketed biologics, operating restriction and criminal prosecutions, delay approval of our product candidates, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and growth prospects. Our future success depends on our ability to manufacture our products, if licensed, on a timely basis with acceptable manufacturing costs, while at the same time maintaining good quality control and complying with applicable regulatory requirements, and an inability to do so could have a material adverse effect on our business, financial condition, and results of operations. In addition, we could incur higher manufacturing costs if manufacturing processes or standards change, and we could need to replace, modify, design, or build and install equipment, all of which would require additional capital expenditures. Specifically, because our product candidates may have a higher cost of goods than conventional therapies, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater.

The manufacture of viral vectors is complex and variable, and there are a limited number of manufacturers able to supply us with viral vectors.

Our DSG3-CAART and MuSK-CAART product candidates utilize a lentiviral delivery vector and some or all of our other product candidates may require a lentiviral delivery vector, a key drug substance that delivers the CAAR to the target T cells. We do not have the capability to manufacture lentiviral vector and plan to obtain the vector we require from third parties. The manufacturing process for lentiviral vector is variable and still evolving. It is not uncommon for manufacturing runs to fail, whether due to contamination, supplier error, or equipment failure, or to be delayed. To the extent our product candidates use a lentiviral delivery vector, a lack of vector supply will cause us to be unable to manufacture our CAAR T cells as well as a delay in patient enrollment, which may have a negative impact on our ability to successfully develop our product candidates.

Further, there are a limited number of manufacturers capable of producing lentiviral vectors. It can be challenging to secure a relationship with any of these manufacturers, and the manufacturing and release process can take a significant amount of time. We have secured a supply of lentiviral vector from CHOP sufficient for a portion of the patients we plan to enroll in our DesCAARTes ™ trial. We have also reserved additional vector manufacturing capacity at Penn and CHOP andin December 2021, we secured a license and supply agreement with Oxford Biomedica to establish a process and supply lentiviral vector for the clinical and commercial development of our DSG3-CAART candidate. There is no assurance that we will be able to secure adequate and timely supply of lentiviral vector. Moreover, we cannot be certain that our CAAR T cell product candidates produced with lentiviral vector from different manufacturers will be comparable or that results of clinical trials will be consistent if conducted with lentiviral vector from different manufacturers.

Vector production also requires the production of high-quality DNA plasmids, for which there is also a limited number of suppliers. Although we have established relationships with multiple suppliers for lentiviral vector and plasmids, we do not yet have our own clinical-scale manufacturing facility established, and are therefore highly

dependent on the ability of these suppliers to manufacture necessary materials and to deliver these materials to us on a timely and reliable basis.

If we are to operate our own manufacturing facility, significant resources will be required and we may fail to successfully operate our facility, which could adversely affect our clinical trials and the commercial viability of our product candidates.

If we establish our own manufacturing facility, our operations will be subject to review and oversight by the FDA and the FDA could object to our use of our manufacturing facility. We must first receive approval from the FDA prior to licensure to manufacture our product candidates, which we may never obtain. Even if licensed, we would be subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMPs and other government regulations. Our license to manufacture product candidates will be subject to continued regulatory review.

Our cost of goods development is at an early stage. The actual cost to manufacture and process our product candidates could be greater than we expect and could materially and adversely affect the commercial viability of our product candidates.

The manufacture of biopharmaceutical products is complex and requires significant expertise, and can be impacted by resource constraints, labor disputes and workforce limitations.

The manufacture of biopharmaceutical products is complex and requires significant expertise, including the development of advanced manufacturing techniques and process controls. Manufacturers of cell therapy products often encounter difficulties in production, particularly in scaling out and validating initial production and ensuring the absence of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if contaminants are discovered in our supply of product candidates or in the manufacturing facilities upon which we currently or will rely, 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 stability or other issues relating to the manufacture of our product candidates, whether by Penn, by a third-party CMO, or at any manufacturing facility that we may establish, will not occur in the future.

Penn, third-party CMOs that we engage or we may fail to manage the logistics of storing and shipping our product candidates. Storage failures and shipment delays and problems caused by us, our vendors or other factors not in our control, such as weather, could result in loss of usable product or prevent or delay the delivery of product candidates to patients.

Penn, third-party CMOs that we engage, or we may also experience manufacturing difficulties due to resource constraints, labor disputes or workforce limitations arising from the expanding need for manufacturing in the cell therapy field and the limited number of training programs for technical staff. If we were to encounter any of these difficulties, our ability to provide our product candidates to patients would be jeopardized.

We are dependent upon the availability of specialty raw materials and the production capabilities of small manufacturers to source the components of our product candidates.

Our product candidates require many specialty raw materials, some of which are manufactured by small companies with limited resources and experience to support a commercial product, and the suppliers may not be able to deliver raw materials to our specifications. In addition, those suppliers generally do not have the capacity to support commercial products manufactured under cGMP by biopharmaceutical firms. The suppliers may be ill-equipped to support our needs, especially in non-routine circumstances like an FDA inspection or medical crisis, such as widespread contamination. We also do not have contracts with many of these suppliers, and we may not be able to contract with them on acceptable terms or at all. Accordingly, we may experience delays in receiving key raw materials to support clinical or commercial manufacturing.

In addition, some raw materials are currently available from a single supplier, or a small number of suppliers. We cannot be sure that these suppliers will remain in business or that they will not be purchased by one of our competitors or another company that is not interested in continuing to produce these materials for our intended purpose. In addition, the lead time needed to establish a relationship with a new supplier can be lengthy, and we may experience delays in meeting demand in the event we must switch to a new supplier. The time and effort to qualify a new supplier could result in additional costs, diversion of resources or reduced manufacturing yields, any of which would negatively impact our operating results. Further, we may be unable to enter into agreements with a new supplier on commercially reasonable terms, which could have a material adverse impact on our business. We are also unable to predict how changing global economic conditions or global health concerns such as the ongoing COVID-19 pandemic will affect our third-party suppliers and manufacturers. Since the beginning of the COVID-19 pandemic, three vaccines for COVID-19 have received Emergency Use Authorization by the FDA and two of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. Any negative impact of such matters on our third-party suppliers and manufacturers may also have an adverse impact on our results of operations or financial condition.

We may encounter difficulties in production, particularly with respect to process development or scaling up of our manufacturing capabilities. If we encounter such difficulties, our ability to provide supply of our CAAR T cells for clinical trials or for commercial purposes could be delayed or stopped.

Establishing clinical and commercial manufacturing and supply is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, increased costs, potential problems with process scale-out, process reproducibility, stability issues, lot consistency, and timely availability of reagents or raw materials. For example, we may find it difficult to establish a manufacturing process that is consistent. If this occurs, we may need to complete more than one manufacturing run for each treated patient, which would impact the availability of adequate coverage and reimbursement from third-party payors. Competitors that have developed CAR T cell therapies have had difficulty reliably producing engineered T cell therapies in the commercial setting. If we experience similar challenges manufacturing product candidates to approved specifications, this may limit our product candidates' utilization and our ability to receive payment for these product candidates once licensed. Alternatively, these challenges may require changes to our manufacturing processes, which could require us to perform additional clinical studies, incurring significant expense. We may ultimately be unable to reduce the expenses associated with our product candidates to levels that will allow us to achieve a profitable return on investment.

If we or our third-party suppliers use hazardous, non-hazardous, biological or other materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials. We and our suppliers are subject to federal, state and local laws and regulations in the United States governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that we and our suppliers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we and our suppliers cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

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

As product candidates are developed through preclinical studies to later-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods or formulation, are altered along the way in an effort to optimize processes and results. Any of these changes could

cause our product candidates to perform differently and affect the results of ongoing and planned clinical trials or other future clinical trials conducted with the altered materials or with materials made with the altered methods. Such changes may also require additional testing, or notification to, or approval by the FDA or other regulatory authorities. This could delay completion of clinical trials, require the conduct of bridging clinical trials or studies, require the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and/or jeopardize our ability to commence product sales and generate revenue.

Risks Related to Government Regulation

The FDA regulatory approval process is lengthy and time-consuming, and we may experience significant delays in the clinical development and regulatory approval of our product candidates.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products, including biologics, are subject to extensive regulation by the FDA and other regulatory authorities in the United States. We are not permitted to market any biological drug product in the United States until we receive approval of a Biologics License Application, or BLA, from the FDA. We have not previously submitted a BLA to the FDA, or similar licensure filings to comparable foreign authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety, potency and purity for each desired indication. The BLA must also include significant information regarding the chemistry, manufacturing and controls for the product, including with respect to chain of identity and chain of custody of the product.

We expect the novel nature of our product candidates to create further challenges in obtaining regulatory approval. For example, the FDA has not previously reviewed regulatory applications for the commercial development of CAAR T cells for treatment of pemphigus, and there is no cell therapy currently approved by the FDA for the treatment of mPV or MuSK myasthenia gravis. Because of this, we have little guidance as to which endpoints will be accepted, how many clinical trials we may expect to conduct, and whether open-label clinical trials will be deemed acceptable, among other things. We may also request regulatory approval of future CAAR T cell-based product candidates by target, regardless of disease type or origin, which the FDA may have difficulty accepting if our clinical trials only involved diseases of certain origins. The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety, potency and purity data to support licensure. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain licensure of the product candidates based on the completed clinical trials, as the FDA often adheres to the Advisory Committee's recommendations. Further, given the rapidly evolving landscape of cell therapy, we could encounter a significant change in the regulatory environment for our product candidates once we have already begun one or more lengthy and expensive clinical trials for our product candidates. Accordingly, the regulatory approval pathway for our product candidates may be uncertain, complex, expensive and lengthy, and approval may not be obtained.

We may also experience delays in completing ongoing and planned clinical trials for a variety of reasons, including delays related to:

- obtaining regulatory authorization to begin a trial, if applicable;
- the availability of financial resources to commence and complete the planned trials;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval at each clinical trial site by an independent IRB;
- recruiting suitable patients to participate in a trial;
- having patients complete a trial, including having patients enrolled in clinical trials dropping out of the trial before the product candidate is manufactured and returned to the site, or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- addressing any patient safety concerns that arise during a trial;

- adding new clinical trial sites; or
- manufacturing sufficient quantities of qualified materials under cGMPs and applying them on a patient by patient basis for use in clinical trials.

We could also encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. If we experience delays in the completion of, any future clinical trial of our product candidates, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may ultimately lead to the denial of regulatory approval of our product candidates.

We expect the product candidates we develop will be regulated as biological products, or biologics, and therefore they may be subject to competition.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, was enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to a licensed biologic. Under the BPCIA, an application for a biosimilar product cannot be licensed by the FDA until 12 years after the reference product was licensed under a BLA. The law is complex and is still being interpreted and implemented by the FDA.

We believe that any of the product candidates we develop that is licensed in the United States as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once licensed, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

The regulatory landscape that will govern our product candidates is uncertain; regulations relating to more established cell therapies and other therapies for B cell-mediated autoimmune diseases are still developing, and changes in regulatory requirements could result in delays or discontinuation of development of our product candidates or unexpected costs in obtaining regulatory approval.

Because we are developing novel CAAR T cell product candidates that are unique biological entities, the regulatory requirements that we will be subject to are not entirely clear. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. For example, regulatory requirements governing gene therapy products and cell therapy products have changed frequently and may continue to change in the future. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies, formerly known as the Office of Cellular, Tissue and Gene Therapies, within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. In addition, under guidelines issued by the National Institutes of Health, or NIH, gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. Before a clinical trial can begin at any institution, that institution's institutional review board, or IRB, and its IBC assesses the safety of the research and identifies any potential risk to public health or the environment. While the NIH guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. Although the FDA decides whether individual gene therapy protocols may proceed, review process and determinations of other reviewing bodies

can impede or delay the initiation of a clinical study, even if the FDA has reviewed the study and approved its initiation. Conversely, the FDA can place an IND application on clinical hold even if such other entities have provided a favorable review. Furthermore, each clinical trial must be reviewed and approved by an independent IRB at or servicing each institution at which a clinical trial will be conducted. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory bodies to change the requirements for approval of any of our product candidates.

Complex regulatory environments exist in other jurisdictions in which we might consider seeking regulatory approvals for our product candidates, further complicating the regulatory landscape. For example, in the European Union, a special committee called the Committee for Advanced Therapies was established within the EMA in accordance with Regulation (EC) No 1394/2007 on advanced-therapy medicinal products, or ATMPs, to assess the quality, safety and efficacy of ATMPs, and to follow scientific developments in the field. ATMPs include gene therapy products as well as somatic cell therapy products and tissue engineered products. These various regulatory review committees and advisory groups and new or revised guidelines that they promulgate from time to time may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. Because the regulatory landscape for our CAAR T cell product candidates is new, we may face even more cumbersome and complex regulations than those emerging for gene therapy products and cell therapy products. Furthermore, even if our product candidates obtain required regulatory approvals, such approvals may later be withdrawn because of changes in regulations or the interpretation of regulations by applicable regulatory agencies. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States. Before we can commercialize any of our product candidates, we must obtain marketing approval. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction and it is possible that none of our product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. We, as a company, have no experience in filing and supporting the applications necessary to gain regulatory approvals and expect to rely on third-party CROs and/or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the drug candidate's safety, potency and purity.

Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining regulatory approvals is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted IND, BLA or equivalent application types, may cause delays in the approval or rejection of an application. The FDA has substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Our

product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA that a drug candidate is safe, potent and pure for its proposed indication or a related companion diagnostic is suitable to identify appropriate patient populations;
- the results of clinical trials may not meet the level of statistical significance required by the FDA for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an BLA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA may fail to approve the manufacturing processes, test procedures and specifications, or facilities that we may establish or of third-party manufacturers with which we may contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA may significantly change in a manner rendering our clinical data insufficient for approval.

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

We expect the novel nature of our product candidates to create further challenges in obtaining regulatory approval. As a result, our ability to develop product candidates and obtain regulatory approval may be significantly impacted. For example, the general approach for FDA approval of a new biologic or drug is for sponsors to seek licensure or approval based on dispositive data from well-controlled, Phase 3 clinical trials of the relevant product candidate in the relevant patient population. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and take years to complete. We believe that we may be able to utilize the FDA's Regenerative Medicine Advanced Therapy designation for our product candidates given the limited alternatives for treatments for certain rare diseases and B cell-mediated autoimmune diseases, but the FDA may not agree with our plans.

Moreover, approval of genetic or biomarker diagnostic tests may be necessary to advance some of our product candidates to clinical trials or potential commercialization. In the future, regulatory agencies may require the development and approval of such tests. Accordingly, the regulatory approval pathway for such product candidates may be uncertain, complex, expensive and lengthy, and approval may not be obtained.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, if licensed, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Even though we may apply for orphan drug designation for our product candidates, we may not be able to obtain orphan drug marketing exclusivity.

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population of 200,000 or more in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. In order to obtain orphan drug designation, the request must be made before submitting a BLA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval of that particular product for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a BLA, to market the same biologic (meaning, a product with the same principal molecular structural features) for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. As a result, even if one of our product candidates receives orphan exclusivity, the FDA can still approve other biologics that do not have the same principal molecular structural features for use in treating the same indication or disease or the same biologic for a different indication or disease during the exclusivity period. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product or if a subsequent applicant demonstrates clinical superiority over our product.

We have obtained from the FDA orphan drug designation for DSG3-CAART for the treatment of pemphigus vulgaris (PV). We may seek orphan drug designation for certain other of our product candidates, but may be unable to obtain orphan drug designation for some or all of our product candidates in specific orphan indications in which we believe there is a medically plausible basis for the use of these products. Even if we obtain orphan drug designation, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition, or if a subsequent applicant demonstrates clinical superiority over our products, if licensed. Although we may seek orphan drug designation for other product candidates, we may never receive such designations. In addition, the FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

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

If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA fast track designation for a particular indication. Fast track is a process designed to facilitate the development, and expedite the review of drugs to treat serious or life-threatening conditions and address an unmet medical need. We have received fast track designation for DSG3-CAART for improving healing of mucosal blisters in patients with mPV. We have also received fast track designation for MuSK-CAART for improving activities of daily living and muscle strength in patients with MuSK antibody-positive myasthenia gravis. We may also apply for fast track designation for certain of our other product candidates, but there is no assurance that the FDA will grant this status to any of our other current or future product candidates. Marketing applications filed by sponsors of products in fast track development may qualify for priority review under the policies and procedures offered by the FDA, but the fast track designation does not assure any such qualification or ultimate marketing approval by the FDA. The FDA has broad discretion whether or not to

grant fast track designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even though we have received fast track designation for DSG3-CAART for improving healing of mucosal blisters in patients with mPV and for MuSK-CAART for improving activities of daily living and muscle strength in patients with MuSK antibody-positive myasthenia gravis, we may not experience a faster development process, regulatory review or approval compared to conventional FDA procedures, and receiving a fast track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. In addition, the FDA may withdraw any fast track designation at any time.

Although we may pursue expedited regulatory approval pathways for a product candidate, it may not qualify for expedited development or, if it does qualify for expedited development, it may not actually lead to a faster development or regulatory review or approval process.

Although we believe there may be an opportunity to accelerate the development of certain of our product candidates through one or more of the FDA's expedited programs, such as fast track, breakthrough therapy, Regenerative Medicine Advanced Therapy, accelerated approval or priority review, we cannot be assured that any of our product candidates will qualify for such programs.

For example, we may seek a Regenerative Medicine Advanced Therapy, or RMAT, designation for some of our product candidates. An RMAT is defined as cell therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products. Gene therapies, including genetically modified cells that lead to a durable modification of cells or tissues may meet the definition of a Regenerative Medicine Therapy. The RMAT program is intended to facilitate efficient development and expedite review of RMATs, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition. A new drug application or a BLA for an RMAT may be eligible for priority review or accelerated approval through (1) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit or (2) reliance upon data obtained from a meaningful number of sites. Benefits of such designation also include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A Regenerative Medicine Therapy that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval. Although RMAT designation or access to any other expedited program may expedite the development or approval process, it does not change the standards for approval. If we apply for RMAT designation or any other expedited program for our product candidates, the FDA may determine that our proposed target indication or other aspects of our clinical development plans do not qualify for such expedited program. Even if we are successful in obtaining a RMAT designation or access to any other expedited program, we may not experience faster development timelines or achieve faster review or approval compared to conventional FDA procedures. Access to an expedited program may also be withdrawn by the FDA if it believes that the designation is no longer supported by data from our clinical development program. Additionally, qualification for any expedited review procedure does not ensure that we will ultimately obtain regulatory approval for such product candidate.

Disruptions at the FDA, the SEC and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those 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 drugs or biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including most recently from December 22, 2018 to January 25, 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Since March 2020 when foreign and domestic inspections were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Since April 2021, the FDA has conducted limited inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Ongoing travel restrictions and other uncertainties continue to impact oversight operations both domestic and abroad and it is unclear when standard operational levels will resume. The FDA is continuing to complete mission-critical work, prioritize other higher-tiered inspectional needs (e.g., for-cause inspections), and carry out surveillance inspections using risk-based approaches for evaluating public health. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, FDA has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. Additionally, during the COVID-19 public health emergency, FDA noted it is working to ensure timely reviews of applications for medical products in line with its user fee performance goals. However, the FDA may not be able to continue its current pace and approval timelines could be extended. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

Risks Related to Ongoing Regulatory Obligations

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

Any regulatory approvals that we receive for our product candidates will require surveillance to monitor the safety, potency and purity of the product candidate. We believe it is likely that the FDA will require a Risk Evaluation and Mitigation Strategy, or REMS, in order to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any BLA, other marketing application and previous responses to inspectional observations. Additionally, manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations and applicable product tracking and tracing requirements. 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. In addition, the FDA could require us to conduct another study to obtain additional safety or biomarker information.

Further, we will be required to comply with FDA promotion and advertising rules, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved uses (known as "off-label use"), limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet and social media. Later discovery of previously unknown problems with our product candidates through follow-up programs with our clinical trial patients, including adverse events of unanticipated severity or frequency, or with our third-party suppliers or 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 our product candidates, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies 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. For example, certain policies of the current U.S. President's administration may impact our business and industry. Namely, the current U.S. President's administration has taken several executive actions, including the issuance of a number of Executive Orders, that could, for example, result in changes to the FDA's priorities and allocation of resources to respond to the COVID-19 pandemic. It is difficult to predict how these orders will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose restrictions on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

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

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

current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to comply with the laws of the FDA, provide true, complete and accurate information to the FDA, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws, or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs.

Risks Related to Healthcare

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

Successful commercialization of our product candidates, if licensed, will depend in part on the extent to which reimbursement for those drug products will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drug products they will pay for and establish reimbursement levels. The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford a drug product. Sales of drug products depend substantially, both domestically and abroad, on the extent to which the costs of drugs products are paid for by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. Any product candidate for which we seek regulatory approval and reimbursement will need to meet or surpass our target product profile, or TPP, to be deemed a viable alternative to currently approved therapies. In addition, because our product candidates represent new approaches to the treatment of B cell-mediated autoimmune diseases, we cannot accurately estimate the potential revenue from our product candidates. *See section entitled "Business — Government Regulation — Pricing and Reimbursement."*

Third-party payors decide which drugs and treatments they will cover and the amount of reimbursement. Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor's determination that use of a product is:

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

Obtaining coverage and reimbursement of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide the payor with supporting scientific, clinical and cost-effectiveness data for the use of our products, if licensed. In the United States, the principal decisions about reimbursement for new drug products are typically made by the Centers for Medicare and Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent a new drug product will be covered and reimbursed under Medicare, and private payors tend to follow CMS to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists among third-party payors and coverage and reimbursement levels for drug products can differ significantly from payor to payor. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Even if we obtain coverage for a given product, if the resulting reimbursement rates are insufficient, hospitals may not approve our product for use in their facility or third-party payors may require co-payments that patients find unacceptably high. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. Separate reimbursement for the product itself may or may not be available. Instead, the hospital or administering physician may be reimbursed only for providing the treatment or procedure in which our product is used. Further, from time to time, CMS revises the reimbursement systems used to reimburse health care providers, including the Medicare Physician Fee Schedule and Outpatient Prospective Payment System, which may result in reduced Medicare payments. In some cases, private third-party payors rely on all or portions of Medicare payment systems to determine payment rates. Changes to government healthcare programs that reduce payments under these programs may negatively impact payments from private third-party payors, and reduce the willingness of physicians to use our product candidates.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if government and other third-party payors fail to provide coverage and adequate reimbursement. We expect downward pressure on pharmaceutical pricing to continue. Further, coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

In the United States, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay regulatory approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain regulatory approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products. *See section entitled "Business — Government Regulation — Other Healthcare Laws and Compliance Requirements — Current and Future Legislation."*

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. 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. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at containing or lowering the cost of healthcare. For example, in 2016, the United Kingdom referendum on its membership in the EU resulted in a majority of the United Kingdom voters voting to exit the EU, often referred to as "Brexit". Pursuant to Article 50 of the Treaty on European Union, the United Kingdom ceased being a Member State of the European Union on January 31, 2020. A transition period began February 1, 2020 and continued until December 31, 2020, during which most laws of the EU continued to apply to the United Kingdom, including the European Union's rules, the European Union's pharmaceutical laws. The United Kingdom and the EU have signed a EU-UK Trade and Cooperation Agreement, which became provisionally applicable on January 1, 2021

and went into force permanently on May 1, 2021, following formal approval by both the United Kingdom and the EU. This agreement provides details on how some aspects of the United Kingdom's and EU's relationship will operate going forwards however there are still many uncertainties. Brexit has already and may continue to adversely affect European and/or worldwide regulatory conditions. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations in Europe, including those related to the pricing of prescription pharmaceuticals, as the United Kingdom determines which EU laws to replicate or replace, which could impair our ability to transact business in the EU and the United Kingdom in the future, if we elect to seek regulatory approval and commercialize any of our products there, if approved. 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. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products, if licensed;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

Our relationships with customers, healthcare providers, physicians, and third-party payors will be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we or our employees, independent contractors, consultants, commercial partners and vendors violate these laws, we could face substantial penalties.

These laws may impact, among other things, our clinical research program, as well as our proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare items and services is subject to extensive laws and regulations designed to prevent fraud, kickbacks, self-dealing and other abusive practices, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute pharmaceutical products. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive and other business arrangements. We may also be subject to federal, state and foreign laws governing the privacy and security of individual identifiable health information and other personally identifiable information. *See section entitled "Business — Government Regulation — Other Healthcare Laws and Compliance Requirements."*

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

The failure to comply with any of these laws or regulatory requirements subjects entities to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, possible

exclusion from participation in federal and state funded healthcare programs, contractual damages and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Any action for violation of these laws, even if successfully defended, could cause a pharmaceutical manufacturer to incur significant legal expenses and divert management's attention from the operation of the business. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities, or our arrangements with physicians, some of whom receive stock options as compensation, could be subject to challenge under one or more of such laws. If we or our employees, independent contractors, consultants, commercial partners and vendors violate these laws, we may be subject to investigations, enforcement actions and/or significant penalties. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter employee misconduct or business noncompliance, and the precautions we take to detect and prevent inappropriate conduct 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. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Related to Data and Privacy

Data collection is governed by restrictive regulations governing the use, processing, and cross-border transfer of personal information.

We are subject to stringent privacy and data protection requirements and these requirements may become more complex as we grow our business and begin to operate in other jurisdictions. For example, the collection, use, storage, disclosure, transfer, or other processing of personal data, including health-related information, regarding individuals in the European Economic Area, or EEA, is governed by the European General Data Protection Regulation, or the GDPR, which became effective on May 25, 2018. The GDPR applies to any business, regardless of its location, that provides goods or services to residents in the EU or monitors the behavior of individuals within the European Union. The GDPR is wide ranging in scope and imposes stringent operational requirements for processors and controllers of personal data, including, for example, special protections for "sensitive information" which includes health and genetic information, expanded disclosures to individuals about how their personal data is to be used, limitations on retention of information, increased requirements pertaining to health data and pseudonymized (*i.e.*, key-coded) data, implementing safeguards to protect the security and confidentiality of personal data, mandatory data breach notification requirements and higher standards for controllers to demonstrate that they have obtained valid consent for certain data processing activities. The GDPR grants individuals the opportunity to object to the processing of their personal information, allows them to request deletion of personal information in certain circumstances, and provides the individual with an express right to seek legal remedies in the event the individual believes his or her rights have been violated. Further, the GDPR imposes strict rules on the transfer of personal data out of the European Union to the United States and other jurisdictions that have not been deemed to offer "adequate" privacy protections.

In addition to the requirement of the GDPR, European Union Member States may make their own further laws and regulations in relation to the processing of genetic, biometric or health data, which could result in differences between Member States, limit our ability to use and share personal data or could cause our costs to increase, and harm our business and financial condition. Should we commence clinical trial activity within the member states of the European Union, such activity will be regulated by the GDPR as well as applicable member state laws. In addition, we are subject to evolving and strict rules on the transfer of personal data out of the European Union to the United

States. For example, evolution of laws governing the cross-border transfer of data, such as the invalidation of the EU–U.S. Privacy Shield, creates additional uncertainty around the legality and mechanics of such transfers. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any future European activities. We could be adversely affected if we fail to comply fully with all of these requirements. Failure to comply with European Union data protection laws may result in fines (for example, of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year (whichever is higher) under the GDPR) and other administrative penalties, which may be onerous and adversely affect our business, financial condition, results of operations and prospects.

In addition, further to the United Kingdom's (UK) exit from the EU on January 31, 2020, the GDPR ceased to apply in the UK at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law (referred to as the 'UK GDPR'). The UK GDPR and the UK Data Protection Act 2018 set out the UK's data protection regime, which is independent from but aligned to the EU's data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. Although the UK is regarded as a third country under the EU's GDPR, the European Commission has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

This lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations could add legal risk, uncertainty, complexity and cost to our handling of EU personal information and our privacy and data security compliance programs. It is possible that over time the UK Data Protection Act could become less aligned with the EU General Data Protection Regulation, or GDPR, which could require us to implement different compliance measures for the UK and the European Union and result in potentially enhanced compliance obligations for EU personal data.

In the United States, there has been a flurry of activity at the state level. In California, the California Consumer Privacy Act, or CCPA, was enacted in June 2018, became effective on January 1, 2020, and became subject to enforcement by the California Attorney General's office on July 1, 2020. The CCPA broadly defines personal information, and creates new individual privacy rights and protections for California consumers (as defined in the law), places increased privacy and security obligations on entities handling personal data of consumers or households, and provides for civil penalties for violations and a private right of action for data breaches. The CCPA requires covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. While there is an exception for protected health information that is subject to HIPAA and clinical trial regulations, the CCPA may impact our business activities if we become a "Business" regulated by the scope of the CCPA.

In addition to the CCPA, new privacy and data security laws have been proposed in more than half of the states in the U.S. and in the U.S. Congress, reflecting a trend toward more stringent privacy legislation in the U.S., which trend may accelerate depending on the new U.S. presidential administration. The effects of the CCPA, and other similar state or federal laws, are potentially significant and may require us to modify our data processing practices and policies and to incur substantial costs and potential liability in an effort to comply with such legislation.

Further, various jurisdictions around the world continue to propose new laws that regulate the privacy and/or security of certain types of personal data. Complying with these laws, if enacted, would require significant resources and leave us vulnerable to possible fines and penalties if we are unable to comply. The regulatory framework governing the collection, processing, storage, use and sharing of certain information is rapidly evolving and is likely to continue to be subject to uncertainty and varying interpretations. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our existing data management practices or the features of our services and platform capabilities. Any failure or perceived failure by us, or any third parties with which we do business, to comply with our posted privacy policies, evolving laws, rules and regulations, industry standards, or contractual obligations to which we or such third parties are or may become subject, may result in actions or other claims against

us by governmental entities or private actors, the expenditure of substantial costs, time and other resources or the incurrence of significant fines, penalties or other liabilities. In addition, any such action, particularly to the extent we were found to be guilty of violations or otherwise liable for damages, would damage our reputation and adversely affect our business, financial condition and results of operations.

If our security measures are breached or unauthorized access to individually identifiable health information or other personally identifiable information is otherwise obtained, our reputation may be harmed, and we may incur significant liabilities.

Unauthorized access to, or security breaches of, our systems and databases could result in unauthorized access to data and information and loss, compromise or corruption of such data and information. The systems of Penn, any CMOs that we may engage in the future, and present and future CROs, contractors and consultants also could experience breaches of security leading to the exposure of confidential and sensitive information. Cyber incidents have been increasing in sophistication and frequency and can include third parties gaining access to employee or customer data using stolen or inferred credentials, computer malware, viruses, spamming, phishing attacks, ransomware, card skimming code, and other deliberate attacks and attempts to gain unauthorized access. Because the techniques used by computer programmers who may attempt to penetrate and sabotage our network security or our website change frequently and may not be recognized until launched against a target, we may be unable to anticipate these techniques.

It is also possible that unauthorized access to customer data may be obtained through inadequate use of security controls by customers, suppliers or other vendors. While we are not currently aware of any impact that the SolarWinds supply chain attack had on our business, this is a recent event, and the scope of the attack is yet unknown. Therefore, there is residual risk that we may experience a security breach arising from the SolarWinds supply chain attack.

In the event of a security breach, our company could suffer loss of business, severe reputational damage adversely affecting investor confidence, regulatory investigations and orders, litigation, indemnity obligations, damages for contract breach, penalties for violation of applicable laws or regulations, significant costs for remediation and other liabilities. For example, the loss of preclinical study or clinical trial data from completed or future preclinical studies or clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

We have incurred and expect to incur significant expenses to prevent security breaches, including costs related to deploying additional personnel and protection technologies, training employees, and engaging third-party solution providers and consultants. Although we expend significant resources to create security protections that shield our customer data against potential theft and security breaches, such measures cannot provide absolute security. Moreover, as we outsource more of our information systems to vendors and rely more on cloud-based information systems, the related security risks will increase, and we will need to expend additional resources to protect our technology and information systems.

We have in the past experienced security incidents, and we may in the future experience other data security incidents or breaches affecting personally identifiable information or other confidential business information. For example, in 2019, we believe a phishing incident led to certain employee email accounts being accessed by an unauthorized third party. We initiated an investigation to determine whether further action was required under applicable law. The incident did not have a material impact on our business or financial condition. While we believe we responded appropriately, including implementing remedial measures with the goal of preventing similar such events in the future, there can be no assurance that we will be successful in these remedial and preventative measures or in successfully mitigating the effects of potential future incidents or cyber-attacks. We remain at risk for future breaches, including, without limitation, breaches that may occur as a result of third-party action, or employee, vendor or contractor error or malfeasance and other causes. If, in the future, we experience a data breach or security incident, we would be likely to experience harm to our reputation, financial performance, and customer and vendor relationships, and the possibility of litigation or regulatory investigations or actions by state and federal governmental authorities and non-U.S. authorities. Additionally, actual, potential or anticipated attacks may cause us to incur increasing costs, including costs to deploy additional personnel and protection technologies, train employees, and

engage third-party experts and consultants. Although we maintain cyber liability insurance, we cannot be certain that our coverage will be adequate for liabilities actually incurred or that insurance will continue to be available to us on economically reasonable terms, or at all.

Interruptions in the availability of server systems or communications with internet or cloud-based services, or failure to maintain the security, confidentiality, accessibility or integrity of data stored on such systems, could harm our business.

We rely upon a variety of internet service providers, third-party web hosting facilities and cloud computing platform providers to support our business. Failure to maintain the security, confidentiality, accessibility or integrity of data stored on such systems could result in interruptions in our operations, damage our reputation in the market, increase our service costs, cause us to incur substantial costs, subject us to liability for damages and/or fines, and divert our resources from other tasks, any one of which could materially adversely affect our business, financial condition, results of operations and prospects. If our security measures or those of our third-party data center hosting facilities, cloud computing platform providers, or third-party service partners, are breached, and unauthorized access is obtained to our data or our information technology systems, we may incur significant legal and financial exposure and liabilities.

We also do not have control over the operations of the facilities of our cloud service providers and our third-party web hosting providers, and they also may be vulnerable to damage or interruption from natural disasters, cybersecurity attacks, terrorist attacks, power outages and similar events or acts of misconduct. In addition, any changes in these providers' service levels may adversely affect our ability to meet our requirements and operate our business.

Risks Related to Ownership of Our Common Stock

Risks Related to Ownership Generally

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

As of December 31, 2021, our executive officers, directors, and 5% stockholders beneficially owned, in the aggregate, approximately 42% of our outstanding voting common stock, or 46% of our common stock, assuming all shares of non-voting common stock are converted into voting common stock in accordance with the terms of our Third Amended and Restated Certificate of Incorporation. Accordingly, these stockholders will have the ability to influence us through this ownership position and significantly affect the outcome of all matters requiring stockholder approval. For example, these stockholders may be able to significantly affect the outcome of elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

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

As a public company, we are required to maintain internal control over financial reporting and to report any material weaknesses in such internal controls. The Sarbanes-Oxley Act requires that we evaluate and determine the effectiveness of our internal control over financial reporting and, beginning with our second annual report following our initial public offering, provide a management report on internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm.

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

assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. We have begun the process of documenting, reviewing, and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act. We have begun recruiting additional finance and accounting personnel with certain skill sets that we need as a public company.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes, and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price and make it more difficult for us to effectively market and sell our service to new and existing customers.

The dual class structure of our common stock may limit your ability to influence corporate matters and may limit your visibility with respect to certain transactions.

The dual class structure of our common stock may limit your ability to influence corporate matters. Holders of our common stock are entitled to one vote per share, while holders of our non-voting common stock are not entitled to any votes. Nonetheless, each share of our non-voting common stock may be converted at any time into one share of our common stock at the option of its holder by providing written notice to us, subject to the limitations provided for in our amended and restated certificate of incorporation. Entities affiliated with or managed by Baker Brothers Life Sciences, L.P. and Adage Capital Partners, LP hold an aggregate of 3,912,500 shares of our non-voting common stock pursuant to our Third Amended and Restated Certificate of Incorporation. At any time, upon written notice, these entities could convert a portion of these shares of non-voting common stock into up to an aggregate of 14% of our shares of common stock. Upon 61 days' prior written notice, these entities could convert any or all of their respective shares of non-voting common stock into shares of common stock. Consequently, if holders of our non-voting common stock exercise their option to make this conversion, this will have the effect of increasing the relative voting power of those prior holders of our non-voting common stock, and correspondingly decreasing the voting power of the holders of our common stock, which may limit your ability to influence corporate matters. Additionally, stockholders who hold, in the aggregate, more than 10% of our common stock and non-voting common stock, but 10% or less of our common stock, and are not otherwise a company insider, may not be required to report changes in their ownership due to transactions in our non-voting common stock pursuant to Section 16(a) of the Exchange Act, and may not be subject to the short-swing profit provisions of Section 16(b) of the Exchange Act.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Certain holders of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

On November 10, 2020, we filed a registration statement on Form S-3 (File No. 333-250006) with the SEC, which was declared effective on November 18, 2020, or the Shelf Registration Statement, in relation to the registration of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof for the purposes of selling, from time to time, our common stock, debt securities or other equity securities in one or more offerings. We also simultaneously entered into a Sales Agreement, or the Sales Agreement, with Cowen and Company, LLC, or the Sales Agent, to provide for the offering, issuance and sale of up to an aggregate amount of $75.0 million of our common stock from time to time in "at-the-market" offerings under the Shelf Registration Statement and subject to the limitations thereof. We will pay to the Sales Agent cash commissions of 3.0 percent of the aggregate gross proceeds of sales of common stock under the Sales Agreement. During the year ended December 31, 2021, we sold 4,792,562 shares pursuant to the ATM Program at an average price of $10.38 per share for net proceeds of $48.3 million, after

deducting commissions of $1.4 million. Sales of common stock, debt securities or other equity securities by us may represent a significant percentage of our common stock currently outstanding. If we sell, or the market perceives that we intend to sell, substantial amounts of our common stock under the Shelf Registration Statement or otherwise, the market price of our common stock could decline significantly.

We have also filed registration statements on Form S-8 to register shares issued or reserved for issuance under our equity compensation plans and will file additional registration statements on Form S-8 to register additional shares pursuant to the "evergreen" provisions under our equity compensation plans. Shares registered under these registration statements on Form S-8 can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates and the lock-up agreements described above. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

In addition, certain of our employees, executive officers, and directors may enter into Rule 10b5-1 trading plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 trading plan, a broker executes trades pursuant to parameters established by the employee, director, or officer when entering into the plan, without further direction from the employee, officer, or director. A Rule 10b5-1 trading plan may be amended or terminated in some circumstances. Our employees, executive officers, and directors also may buy or sell additional shares outside of a Rule 10b5-1 trading plan when they are not in possession of material, nonpublic information.

Risks Related to our Charter and Bylaws

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, or by a majority of the total number of authorized directors;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of the holders of not less than 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors;
- a requirement of approval of not less than 75% of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or

potential acquirors to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

Our amended and restated bylaws designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Pursuant to our amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Chancery Court does not have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) will be the sole and exclusive forum for state law claims for: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or bylaws; (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (v) any action asserting a claim governed by the internal affairs doctrine (the Delaware Forum Provision). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act of 1933, as amended (the Securities Act) or the Securities Exchange Act of 1934. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions. We recognize that the forum selection clause in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. The Court of Chancery of the State of Delaware may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition and operating results.

Risks Related to Tax

Changes in tax laws could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. Prospective investors in our common stock should consult with their legal and tax advisors with respect to potential changes in tax laws and the tax consequences of investing in or holding our common stock.

Our ability to utilize our net operating losses and certain other tax attributes to offset future taxable income may be subject to certain limitations.

As of December 31, 2021, we had U.S. federal, state and local net operating loss carryforwards of $85.8 million, $88.0 million and $78.9 million, respectively. $0.3 million of the federal amounts expire in 2037. The state net operating losses begin to expire in 2037 and the local net operating losses begin to expire in 2039. Approximately $85.5 million of the federal net operating losses can be carried forward indefinitely. Certain net operating loss carryforwards could expire unused and be unavailable to offset future taxable income. In addition, in general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its

pre-change net operating loss carryforwards or tax credits, or NOLs or credits, to offset future taxable income or taxes. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a specified testing period. Our existing NOLs or credits may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change, our ability to utilize NOLs or credits could be further limited by Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Our NOLs or credits may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or credits. Furthermore, our ability to utilize our NOLs or credits is conditioned upon our attaining profitability and generating U.S. federal and state taxable income. As described above under "—Risks Related to Our Financial Condition and Capital Requirements", we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; and therefore, we do not know whether or when we will generate the U.S. federal or state taxable income necessary to utilize our NOLs or credits. Under current law, U.S. federal net operating loss carryforwards generated in taxable years beginning after December 31, 2017 will not be subject to expiration. However, any such net operating loss carryforwards may only offset 80% of our annual taxable income in taxable years beginning after December 31, 2020.

General Risk Factors

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

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

- the commencement, enrollment or results of our planned preclinical studies or clinical trials of our product candidates or any preclinical studies or future clinical trials we may conduct, or changes in the development status of our product candidates;
- our decision to initiate a preclinical study or clinical trial, not to initiate a preclinical study or clinical trial or to terminate an existing preclinical study or clinical trial;
- adverse results or delays in preclinical studies or clinical trials of our product candidates;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including, without limitation, the FDA's issuance of a "refusal to file" letter or a request for additional information;
- our failure to commercialize our product candidates;
- adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- changes in laws or regulations applicable to our product candidates, including, but not limited to, clinical trial requirements for approvals;
- adverse developments concerning our manufacturers or suppliers;
- our inability to obtain adequate product supply for any licensed product or inability to do so at acceptable prices;
- our inability to establish collaborations, if needed;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of our product candidates;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;

- our ability to effectively manage our growth;
- the size and growth of our initial target markets;
- our ability to successfully treat additional types of B cell-mediated autoimmune diseases;
- actual or anticipated variations in annual or quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- general political and economic conditions;
- global health concerns, such as the ongoing COVID-19 pandemic; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and The Nasdaq Global Select Market and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations in recent years that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. Securities class action litigation has often been instituted against companies, particularly in the biopharmaceutical and life sciences industries, following periods of volatility in the market price of a company's securities. We have been subject to such a securities class action lawsuit filed in February 2022 against certain of our officers and certain of our current and former directors, and may become subject to additional securities class action lawsuits in the future. *See "Item 3. Legal Proceedings" for more information.* This type of litigation could result in substantial costs and a diversion of management's attention and resources, which would harm our business, operating results or financial condition.

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

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

We are an emerging growth company and a "smaller reporting company," and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act, or JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies,

including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years following the date of completion of our initial public offering, although circumstances could cause us to lose that status earlier. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of our initial public offering, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, we are not subject to the same new or revised accounting standards as other public companies that are not emerging growth companies and our financial statements may not be comparable to other public companies that comply with new or revised accounting pronouncements as of public company effective dates.

We are also a "smaller reporting company," as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended. We would cease to be a smaller reporting company if we have a public float in excess of $250 million, or have annual revenues in excess of $100 million and a public float in excess of $700 million, determined on an annual basis. Consequently, even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates or grant licenses on terms unfavorable to us.

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

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. In the event that one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters are located in Philadelphia, PA, where we lease 7,672 square feet of office, research and development space subject to a lease agreement that is in effect through June 30, 2025. We also have a lease consisting of approximately 3,800 square feet of laboratory space in Philadelphia, PA that can be terminated by us with 90 days' notice. We believe our facilities are currently adequate for us to conduct our business.

Item 3. Legal Proceedings.

From time to time, we may be involved in lawsuits, claims, investigations and proceedings, consisting of intellectual property, commercial, employment and other matters which arise in the ordinary course of business. While the outcome of any such proceedings cannot be predicted with certainty, as of December 31, 2021, we were not party to any legal proceedings that we would expect to have a material adverse impact on our financial position, results of operations or cash flow.

On February 28, 2022, a purported stockholder of the Company filed a complaint against us and certain of our current officers and certain of our current and former directors in the United States District Court for the Eastern District of Pennsylvania captioned *Patterson v. Cabaletta Bio, Inc., et al*.. No. 2:22-cv-00737 (E.D. Pa.). The complaint was filed on behalf of a putative class of persons and entities who purchased or otherwise acquired (a) Cabaletta common stock pursuant and/or traceable to the offering documents issued in connection with the Company's October 24, 2019 initial public offering; and/or (b) Cabaletta securities between October 24, 2019 and December 13, 2021 both dates inclusive. The complaint alleges claims under Sections 10(b) and 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder and under Sections 11 and 15 of the Securities Act based upon allegedly false or misleading statements and omissions regarding our DesCAARTes ™ Phase 1 clinical trial of DSG3-CAART, clinical data for the DesCAARTes™ trial, the efficacy of DSG3-CAART, and the clinical and/or commercial prospects for DSG3-CAART. The complaint seeks damages, prejudgment and post-judgment interest, and reasonable attorneys' fees, expert fees and other costs. We may also become subject to additional securities class action lawsuits in the future. We intend to vigorously defend the lawsuit. At this time, no assessment can be made as to its likely outcome or whether the outcome will be material us. *See Risk Factors — "The price of our stock may be volatile, and you could lose all or part of your investment" for additional information.*

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 trades on The Nasdaq Global Select Market under the symbol "CABA". Trading of our common stock commenced on October 25, 2019, in connection with our initial public offering, or IPO. Prior to that time, there was no established public trading market for our common stock.

Stockholders

As of March 10, 2022, we had approximately 20 holders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. The number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and growth of our business. We do not expect to pay any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects, then applicable contractual restrictions and any other factors deemed relevant by our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividends.

Equity Compensation Plan

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Issuer Purchases of Equity Securities

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

Recent Sales of Unregistered Securities

None.

Item 6. Reserved.

Not applicable.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K, or this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the section entitled "Risk Factors," our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. You should carefully read the section entitled "Risk Factors" to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section entitled "Special Note Regarding Forward-Looking Statements." We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Overview

We are a clinical-stage biotechnology company focused on the discovery and development of engineered T cell therapies, and aim to provide a deep and durable, perhaps curative, treatment, for patients with B cell-mediated autoimmune diseases. Our proprietary technology utilizes Chimeric AutoAntibody Receptor, or CAAR, T cells that are designed to selectively bind and eliminate only specific B cells that produce disease-causing autoantibodies, or pathogenic B cells, while sparing normal B cells. Our lead CAAR T cell product candidate was designed based on the clinically validated and commercially approved Chimeric Antigen Receptor, or CAR, T cell technology that is marketed for the treatment of B cell cancers. By harnessing the power of targeted cell therapy, we believe our CAAR T product candidates have the potential to provide responses that may be a safer and more effective option than current treatments. We believe our technology, in combination with our proprietary Cabaletta Approach for selective B cell Ablation platform, called our CABA™ platform, has applicability across over two dozen B cell-mediated autoimmune diseases that we have identified, evaluated, and prioritized.

Our initial focus is mucosal pemphigus vulgaris, or mPV, which is an autoimmune blistering disease. Our lead product candidate, DSG3-CAART, is being evaluated for the treatment of mPV, a subtype of pemphigus vulgaris, or PV, that affects the mucous membrane. mPV is caused by autoantibodies against the cell adhesion protein desmoglein 3, or DSG3. DSG3-CAART is designed to selectively target and eliminate autoreactive B cells specific for DSG3, which may prevent these B cells from differentiating into antibody secreting plasma cells that produce anti-DSG3 antibodies that are the cause of mPV, while preserving general B cell immune function. DSG3-CAART is being evaluated in a Phase 1 trial, or the DesCAARTes ™ trial, in which we are currently enrolling patients. During 2021, we reported acute and 28-day safety data from the first three cohorts of patients in the DesCAARTes ™ trial, with no dose-limiting toxicities, or DLTs, or clinically relevant adverse events observed in the 28 days after infusion of DSG3-CAART. In November 2021, we reported that dose-dependent increases in DSG3-CAART persistence in the third cohort relative to the first two low dose cohorts throughout the 28 days following infusion had been observed. On December 14, 2021, we reported top-line biologic activity data for the first, two low dose cohorts, where no clear evidence of biologic activity was observed at doses that represent less than 2% of the current planned maximum dose in the trial, as well as the continued absence of any DLTs or clinically relevant adverse events. Furthermore, we announced the addition of a planned fifth cohort to receive a higher dose with a more consolidated dosing regimen, which we expect to initiate in 2022 after review of the fourth cohort's 28-day safety data. In January 2022, we announced that 28-day safety data for the fourth cohort was anticipated to be announced in the first quarter of 2022, and that other clinical data updates from the DesCAARTes ™ trial are expected to be provided at scientific meetings throughout 2022 and 2023 with biologic activity data for cohorts A3 and A4 expected to be announced in mid-2022. In March 2022, we disclosed 28-day safety data for the fourth cohort with no DLTs observed in any patient during the 28 days after infusion of DSG3-CAART. In addition, we disclosed that we are currently enrolling patients for the fifth cohort, and expect to announce 28-day safety data for the fifth cohort at a scientific meeting in mid-2022, assuming no DLTs are observed during such cohort, that enrollment is uninterrupted and there are no delays due to COVID-19 resurgence.

Our MuSK-CAART product candidate is designed for the treatment of muscle-specific kinase myasthenia gravis, or MuSK MG. In the fourth quarter of 2021, we submitted an Investigational New Drug, or IND, application for the first-in-human studies to the United States Food and Drug Administration, or FDA, which became effective in January 2022. In February 2022, MuSK-CAART received fast track designation from the FDA for improving

activities of daily living and muscle strength in patients with MuSK antibody-positive myasthenia gravis. We plan to initiate the MusCAARTes™ trial in 2022. We are also advancing additional product candidates currently in discovery-stage or preclinical development for the treatment of mucocutaneous PV, or mcPV, PLA2R-associated membranous nephropathy, or PLA2R MN, and Hemophilia A with Factor VIII, or FVIII, alloantibodies, in addition to two undisclosed targets. We conducted a pre-IND interaction with the FDA to discuss the development path for PLA2R-CAART in the fourth quarter of 2021. Preclinical data indicating that PLA2R CAAR T cells specifically recognized and eliminated anti-PLA2R antibody-expressing B cells and that membrane proteome arrays screened with PLA2R CAAR candidates did not identify off-target interaction was presented at the American Society of Nephrology Kidney Week in the fourth quarter of 2021.

We were incorporated in April 2017. In August 2018, we entered into multiple agreements with Penn to develop the CAAR T technology to treat B cell-mediated autoimmune diseases. Our operations to date have been financed primarily by net proceeds of $86.4 million from the sale of convertible notes and convertible preferred stock and net proceeds of $71.0 million from the sale of common stock in our initial public offering, or IPO, in October 2019. In 2021, we raised $49.7 million, with net proceeds of $48.3 million, in "at-the-market" offerings, pursuant to a Sales Agreement, or the Sales Agreement, with Cowen and Company, LLC, or the Sales Agent, which provides for the offering, issuance and sale of up to an aggregate amount of $75.0 million of our common stock. As of December 31, 2021, we had $122.2 million in cash and cash equivalents.

Amended and Restated License Agreement with the Trustees of the University of Pennsylvania and the Children's Hospital of Philadelphia

In August 2018, we entered into a license agreement with Penn, which was amended and restated in July 2019 to include the Children's Hospital of Philadelphia, or CHOP, collectively, the Institutions, and collectively with such amendment, as amended in May 2020 and October 2021, the License Agreement, pursuant to which we obtained (a) a non-exclusive, non-sublicensable, worldwide research license to make, have made and use products in two subfields of use, (b) effective as of October 2018, an exclusive, worldwide, royalty-bearing license, with the right to sublicense, under certain of the Institutions' intellectual property to make, use, sell, offer for sale and import products in the same two subfields of use, and (c) effective as of October 2018, a non-exclusive, worldwide, royalty-bearing license, with limited rights to sublicense, under certain of Penn's know-how to make, have made, use, sell, offer for sale, import and have imported products in the same two subfields of use. Our rights are subject to the rights of the U.S. government and certain rights retained by the Institutions.

Unless earlier terminated, the License Agreement expires on the expiration or abandonment or other termination of the last valid claim in Penn's intellectual property licensed by us. We may terminate the License Agreement at any time for convenience upon 60 days written notice. In the event of an uncured, material breach, Penn may terminate the License Agreement upon 60 days written notice.

Sponsored Research Agreements

We have sponsored research agreements, or SRAs, with Penn for the laboratories of Drs. Payne and Milone, who are also our scientific co-founders and members of our scientific advisory board. In May 2020, the agreement with Dr. Payne, or the Payne SRA, was expanded to include CAAR design and optimization efforts in three additional B cell-mediated autoimmune diseases. In August 2020, the Payne SRA was further amended to extend the term of the original research plan. In April 2021 and October 2021, the Milone SRA was amended to extend the term of the original research plan through November 2022. In December 2021, we further amended the Payne SRA to extend the term through December 2024 and expand the workplan to include additional correlative studies related to the DesCAARTes™ trial. The total estimated cost of the agreements is $12.5 million, which satisfies the $2.0 million annual obligation under the License Agreement. As of December 31, 2021, $9.9 million of cost has been incurred pursuant to these agreements.

In December 2021, we entered into a SRA with Penn for the laboratory of Dr. Drew Weissman, or the Weissman SRA. Under the Weissman SRA, discovery-stage proof of concept studies for lipid nanoparticle mRNA for the delivery and/or enhancement of CAAR technology is being conducted. Under the Weissman SRA, Penn granted us a non-transferable, non-exclusive license to use certain intellectual property for specific internal research purposes and further grants us the first option to negotiate to acquire, subject to agreement on commercial terms, an exclusive or

non-exclusive worldwide license to certain patent rights for specific CAAR products developed under the Weissman SRA. Unless earlier terminated, the Weissman SRA will expire in December 2023. Pursuant to the Weissman SRA, we also entered into an Option Agreement with Penn, or the Weissman Option, which grants us the option to negotiate to acquire a non-exclusive worldwide license to certain patent rights in connection with the Weissman SRA.

Master Translational Research Services Agreement

In October 2018, we entered into a Master Translational Services Agreement with Penn, or the Services Agreement, pursuant to which Penn agreed to perform certain services related to the research and development of the technology licensed to us under the License Agreement, as well as certain clinical, regulatory and manufacturing services. The Services Agreement will expire on the later of (i) October 19, 2021 or (ii) completion of the services for which we have engaged Penn under the Services Agreement. Either party may terminate this agreement with or without cause upon a certain number of days' prior written notice. The services encompassed by the Services Agreement are performed by different organizations at Penn pursuant to certain addenda to the Services Agreement, including the Center for Advanced Retinal and Ocular Therapeutics, or CAROT, Addendum, as amended in May 2020, and the CVPF Addendum.

Components of Operating Results

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sales of products for several years, if at all. If our development efforts for our current or future product candidates are successful and result in marketing approval, we may generate revenue in the future from product sales. We cannot predict if, when or to what extent we will generate revenue from the commercialization and sale of our product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates.

We may also in the future enter into license or collaboration agreements for our product candidates or intellectual property, and we may generate revenue in the future from payments as a result of such license or collaboration agreements.

Operating Expenses

Research and Development

Our research and development expenses include:

- personnel costs, which include salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with consultants and third-party contract organizations that conduct research and development activities on our behalf;
- costs related to sponsored research service agreements;
- costs related to production of preclinical and clinical materials, including fees paid to contract manufacturers;
- licensing fees for intellectual property and know-how;
- laboratory and vendor expenses related to the execution of preclinical studies and ongoing and planned clinical trials; and
- laboratory supplies and equipment used for internal research and development activities and related depreciation expense.

We have not reported program costs since inception because historically we have not tracked or recorded our research and development expenses on a preclinical program-by-program basis. We use our personnel and infrastructure resources across the breadth of our research and development activities, which are directed toward identifying and developing product candidates.

We expense all research and development costs in the periods in which they are incurred. Costs for certain research and development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and third-party service providers.

We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates, including investments in manufacturing, as our programs advance and we conduct clinical trials. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

Because of the numerous risks and uncertainties associated with product development, we cannot determine with certainty the duration and completion costs of the current or future preclinical studies and clinical trials or if, when, or to what extent we will generate revenues from the commercialization and sale of our product candidates. We may never succeed in achieving regulatory approval for our product candidates. The duration, costs and timing of preclinical studies and clinical trials and development of our product candidates will depend on a variety of factors, including:

- successful completion of preclinical studies and IND-enabling studies;
- development of chemistry, manufacturing and controls, or CMC, processes and procedures for purposes of IND applications;
- successful patient enrollment in, and the initiation and completion of, clinical trials;
- the impact of any business interruptions to our operations, including the timing and enrollment of patients in our ongoing and planned clinical trials, or to those of our clinical sites, manufacturers, suppliers, or other vendors resulting from the COVID-19 pandemic or similar public health crisis;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety and efficacy profile following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- achieving desirable medicinal properties for the intended indications.

We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our preclinical studies and clinical trials. We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. A change in the outcome of any of these factors could mean a significant change in the costs and timing associated with the development of our current and future preclinical and clinical product candidates. For example, if the FDA or another regulatory authority, were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development, or if we experience significant delays in execution of or enrollment in any of our preclinical studies or clinical trials, we could be required to expend significant additional financial resources and time on the completion of preclinical and clinical development. We expect our research and development expenses to increase for the foreseeable future as we continue the development of product candidates.

General and Administrative Expenses

Our general and administrative expenses consist primarily of personnel costs, costs related to maintenance and filing of intellectual property, depreciation expense and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs consist of salaries, benefits and stock-based compensation expense. We expect our general and administrative expenses to increase over the next several years to support our continued research and development activities, manufacturing activities, increased costs of operating as a public company and the potential commercialization of our product candidates. We anticipate our general and administrative costs will increase with respect to the hiring of additional personnel, developing commercial infrastructure, fees to outside consultants, lawyers and accountants, and increased costs associated with being a public company such as expenses related to services associated with maintaining compliance with Nasdaq listing rules and SEC requirements, insurance and investor relations costs.

Other Income

Other income consists of interest earned on our cash equivalents, amortization of bond discount or premium and investment gains and losses realized during the period.

Results of Operations for the years ended December 31, 2021 and 2020

The following sets forth our results of operations:

	Year Ended December 31,		
	2021	2020	Change
	(in thousands)		
Statements of Operations Data:			
Operating expenses:			
Research and development	$ 32,494	$ 21,376	$ 11,118
General and administrative	13,819	12,457	1,362
Total operating expenses	46,313	33,833	12,480
Loss from operations	(46,313)	(33,833)	(12,480)
Other income:			
Interest income	24	494	(470)
Net loss	$ (46,289)	$ (33,339)	$ (12,950)

Research and Development Expenses

Research and development expenses were $32.5 million for the year ended December 31, 2021 as compared to $21.4 million for the year ended December 31, 2020. The table below summarizes our research and development expenses:

	Year Ended December 31,		
	2021	2020	Change
	(in thousands)		
Sponsored research activities	$ 3,021	$ 3,062	$ (41)
License of intellectual property and subscription fee	28	143	(115)
Manufacturing of preclinical and clinical supplies	7,390	4,652	2,738
Clinical trials	3,165	1,202	1,963
Personnel	10,604	7,827	2,777
Development services	7,933	4,350	3,583
Other	353	140	213
	$ 32,494	$ 21,376	$ 11,118

Specific changes in our research and development expenses year over year include a:

- $3.6 million increase in costs under our development services from increased outsourced preclinical research activities and lab related expenses;
- $2.8 million increase in personnel costs primarily driven by an increase in headcount to support overall growth, including an increase of $0.8 million in stock-based compensation expense;
- $2.7 million increase in manufacturing costs primarily due to vector manufacturing and cell processing capabilities and related activities; and
- $2.0 million increase in clinical trial costs for the DesCAARTes™ trial, including outsourced costs and investigator payments to clinical trial sites.

General and Administrative Expenses

General and administrative expenses were $13.8 million for the year ended December 31, 2021 as compared to $12.5 million for the year ended December 31, 2020. The increase of $1.3 million in our general and administrative expenses year over year includes:

- $1.1 million of additional personnel costs primarily due to an increase of $0.7 million in stock-based compensation expense; and
- $0.2 million of additional services, including legal and other general and administrative expenses.

Other Income

Interest income has decreased $0.5 million for the year ended December 31, 2021 as compared to the year ended December 31, 2020 primarily as a result of a significant decrease in interest rates beginning in March 2020.

Liquidity and Capital Resources

Since our inception in April 2017 through December 31, 2020, our operations have been financed by proceeds of $86.4 million from the sale of convertible notes and our convertible preferred stock and proceeds of $71.0 million from the sale of common stock in our initial public offering. In 2021, we raised $49.7 million, with net proceeds of $48.3 million, in "at-the-market" offerings, pursuant to our Sales Agreement which provides for the offering, issuance and sale of up to an aggregate amount of $75.0 million of our common stock. As of December 31, 2021, we had $122.2 million in cash and cash equivalents. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation.

We have incurred losses since our inception and, as of December 31, 2021, we had an accumulated deficit of $112.6 million. Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures, and to a lesser extent, general and administrative expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding prepaid expenses and other current assets, accounts payable and accrued expenses.

Any product candidates we may develop may never achieve commercialization and we anticipate that we will continue to incur losses for the foreseeable future. We expect that our research and development expenses, general and administrative expenses, and capital expenditures will continue to increase. As a result, until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third-party clinical research, manufacturing and development services, costs relating to the build-out of our headquarters, laboratories and manufacturing facility, license payments or milestone obligations that may arise, laboratory and related supplies, clinical costs, manufacturing costs, legal and other regulatory expenses and general overhead costs.

Based upon our current operating plan, we believe that our existing cash, cash equivalents and investments as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements through the third quarter of 2023. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. We will continue to require additional financing to advance our current product candidates through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. We will continue to seek funds through equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise capital, we will need to delay, reduce or terminate planned activities to reduce costs.

At-The-Market Offering Sales Agreement

On November 10, 2020, we filed a registration statement on Form S-3 (File No. 333-250006) with the SEC, which was declared effective on November 18, 2020, or the Shelf Registration Statement, in relation to the registration of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof for the purposes of selling, from time to time, our common stock, debt securities or other equity securities in one or more offerings. We also simultaneously entered into a Sales Agreement with Cowen and Company, LLC, to provide for the offering, issuance and sale of up to an aggregate amount of $75.0 million of our common stock from time to time in "at-the-market" offerings, or the ATM Program, under the Shelf Registration Statement and subject to the limitations thereof. We will pay to the Sales Agent cash commissions of 3.0 percent of the aggregate gross proceeds of sales of common stock under the Sales Agreement. In 2021, we sold 4,792,562 shares pursuant to the ATM Program for net proceeds of $48.3 million, after deducting commissions of $1.4 million.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the scope, progress, results and costs of researching, developing and manufacturing our lead product candidates or any future product candidates, and conducting preclinical studies and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals or clearances for our lead product candidates or any future product candidates;
- the impact of any business interruptions to our operations or to those of our clinical sites, manufacturers, suppliers, or other vendors resulting from the COVID-19 pandemic or similar public health crisis;
- the number and characteristics of any additional product candidates we develop or acquire;
- the timing of any cash milestone payments if we successfully achieve certain predetermined milestones;
- the cost of manufacturing our lead product candidate or any future product candidates and any products we successfully commercialize, including costs associated with building-out our manufacturing capabilities;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of any such agreements that we may enter into;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company; and
- the timing, receipt and amount of sales of any future approved or cleared products, if any.

Further, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development activities. We currently have no credit facility or committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated product development programs.

Cash Flows

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (34,109)	$ (26,770)
Investing activities	5,999	(7,981)
Financing activities	48,903	(24)
Net increase (decrease) in cash and cash equivalents	$ 20,793	$ (34,775)

Operating Activities

During the year ended December 31, 2021, cash used in operating activities of $34.1 million was attributable to our net loss of $46.3 million, offset by the net change of $5.6 million in our net operating assets and liabilities and non-cash charges of $6.6 million for stock-based compensation charges, amortization of premium on investments and depreciation.

During the year ended December 31, 2020, cash used in operating activities of $26.8 million was attributable to our net loss of $33.3 million, offset by the net change of $1.6 million in our net operating assets and liabilities and non-cash charges of $4.9 million for stock-based compensation charges, amortization of premium on investments and depreciation.

Investing Activities

During the year ended December 31, 2021, cash provided in investing activities of $6.0 million was attributable to proceeds of $7.2 million from maturities of investments, partially offset by $1.2 million of purchases of property and equipment.

During the year ended December 31, 2020, cash used in investing activities of $8.0 million was attributable to $11.1 million of purchases of investments and $0.6 million of purchases of property and equipment, partially offset by proceeds of $3.7 million from maturities of investments.

Financing Activities

During the year ended December 31, 2021, cash provided by financing activities of $48.9 million was from $48.3 million in sales of common stock, net of issuance costs and $0.6 million from stock option exercises and purchases of shares under the 2019 Employee Stock Purchase Plan.

During the year ended December 31, 2020, cash used in financing activities included $0.2 million in payments for common stock issuance costs from our IPO in October 2019, offset by $0.2 million in proceeds from stock option exercises and purchases of shares under the employee stock purchase plan.

Contractual Obligations and Commitments

In February 2019, we entered into an operating lease agreement for office space in Philadelphia, Pennsylvania. The lease term commenced in May 2019 and will expire in July 2022. The initial annual base rent was $0.3 million, and such amount will increase by 2% annually on each anniversary of the commencement date. In February 2022, this lease was amended to extend the term by 35 months, now terminating in June 2025, with annual base rent starting at $0.3M and increasing by 2.5% annually.

In January 2021, we entered into a Development and Manufacturing Services Agreement (WuXi Agreement) with WuXi Advanced Therapies, Inc. (WuXi) to serve as our cell processing manufacturing partner for the planned MuSK-CAART Phase 1 clinical trial, or MusCAARTes ™ trial. We concluded the WuXi Agreement has an embedded lease as a dedicated manufacturing suite is used for our cell processing manufacturing, with a monthly fee of $0.1 million for this suite. The WuXi Agreement will expire the later of January 2024, or upon completion of WuXi's services related to the MusCAARTes ™ trial. We have the right to terminate the WuXi Agreement for convenience or other reasons specified in the WuXi Agreement upon prior written notice. If we terminate the WuXi Agreement, we will be obligated to pay an early termination fee of up to $1.5 million.

Our commitments include:

- *The Penn License Agreement.* Under the License Agreement, we are required to make milestone payments upon successful completion of certain development, regulatory and sales milestones on a product-by-product and geographical basis. The payment obligations under the License Agreement are contingent upon future events such as our achievement of specified development, regulatory and commercial milestones and we will be required to make development milestone payments and royalty payments in connection with the sale of products developed under the License Agreement. As of December 31, 2021, we are unable to estimate the timing or likelihood of achieving the milestones or making future product sales. We were also obligated to pay $2.0 million annually for three years beginning August 2018 for funding to the laboratories of Drs. Payne and Milone.

  Under the License Agreement, we must use commercially reasonable efforts to develop and commercialize a product in each subfield. During the term of the License Agreement until the first commercial sale of the first product, we are obligated to pay Penn a non-refundable, non-creditable annual license maintenance fee of $10,000. We are required to pay certain milestone payments upon the achievement of specified clinical and commercial milestones. Milestone payments are reduced by a certain percentage for the second product that achieves a milestone, by an additional percentage for the third product that achieves a milestone, and so on, for each subsequent product that achieves a milestone. In the event that we are able to successfully develop and launch multiple products under the License Agreement, total milestone payments could be approximately $21.0 million. Penn is also eligible to receive tiered royalties at percentage rates in the low single-digits, subject to an annual minimum royalty, on annual worldwide net sales of any products that are commercialized by us or our sublicensees that contain or incorporate, or are covered by, the intellectual property licensed by us. To the extent we sublicense our license rights under the License Agreement, Penn would be eligible to receive tiered sublicense income at percentage rates in the mid-single to low double-digits. We have also entered into a subscription and technology transfer agreement with Penn, pursuant to which we owed Penn an upfront subscription fee, which was paid in 2019, and a nominal non-refundable royalty on net sales of products, a portion of which will be credited toward milestone payments and royalties under this License Agreement. Technology transfer activities would be at our cost and subject to agreement as to the technology to be transferred.

- *Master Translational Research Services Agreement with Penn.* Under the Services Agreement, we have contracted for additional research and development services from various laboratories within Penn. The Services Agreement will expire upon completion of the services for which we have engaged Penn under the Services Agreement. In May 2020, the Company amended its Addendum with the Center for Advanced Retinal and Ocular Therapeutics (CAROT) to expand access to vector manufacturing. We may incur additional expenses up to $1.4 million through the remaining term of the CAROT Amended Addendum.

- *Sponsored Research Agreements.* We have sponsored research agreements, or SRAs, with Penn for the laboratories of our scientific co-founders Drs. Payne and Milone. In May 2020, the Payne SRA was expanded to include CAAR design and optimization efforts in three additional B cell-mediated autoimmune diseases. In August 2020, this SRA was further amended to extend the term of the original research plan.In December 2021, we further amended the Payne SRA to extend the term through December 2024 and expand the workplan to include additional correlative studies related to the DesCAARTes ™ trial. In April 2021 and October 2021, the Milone SRA was amended to extend the term of the original research plan through November 2022. The total estimated cost of the agreements is $12.5 million, which satisfies the $2.0 million annual obligation under the Penn License Agreement. As of December 31, 2021, $9.9 million of cost has been incurred pursuant to these agreements.
- *Licence and Supply Agreement.* In December 2021, we entered into a Licence and Supply agreement, or LSA, with Oxford Biomedica (UK) Limited wherein the LSA grants us a non-exclusive license to Oxford's LentiVector® platform for its application in our DSG3-CAART program and puts in place a multi-year vector supply agreement. Under the terms of the agreement, we are required to pay Oxford an upfront fee, as well as costs associated with initial vector manufacturing activities for a total cost of up to approximately $4.0 million. Oxford is eligible to receive regulatory and sales milestones in the low tens of millions and royalties in the low single digits on net sales of products that incorporate the Oxford technology. We can terminate the agreement at will upon advance written notice and subject to certain manufacturing slot cancellation fees. As of December 31, 2021, we have recognized expenses of approximately $1.1 million under this LSA.
- *Manufacturing agreement*s. In February 2021, as amended in May 2021, we entered into a research service agreement with CHOP for vector manufacturing for a total cost of $1.7 million. As of December 31, 2021, we expect to incur the remaining cost of approximately $0.6 million through the first half of 2023.

  In August 2021 and October 2021, we entered into agreements with a contract manufacturing organization for the purchase of plasmids to be used in vector manufacturing for a total of cost $1.6 million. As of December 31, 2021, we expect to incur the remaining cost of $0.3 million in the first quarter of 2022.
- *Other Purchase Commitments.* In the normal course of business, we enter into various purchase commitments with third-party contract manufacturers for the manufacture and processing of our product candidates and related raw materials, contracts with contract research organizations for clinical trials and agreements with vendors for other services and products for operating purposes. These agreements generally provide for termination or cancellation other than for costs already incurred.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with generally accepted accounting principles, or GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

While our significant accounting policies are described in more detail in Note 2 to our financial statements appearing elsewhere in this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Research and Development Costs

We estimate costs of research and development activities conducted by service providers, which include activities under the Penn License Agreement, the conduct of sponsored research, preclinical studies and contract

manufacturing activities. We record the estimated costs of research and development activities based upon the estimated amount of services provided and include these costs in the accrued and other current liabilities or prepaid expenses on the balance sheets and within research and development expense on the statements of operations.

We estimate these costs based on factors such as estimates of the work completed and budget provided and in accordance with agreements established with our collaboration partners and third-party service providers. We make significant judgments and estimates in determining the accrued liabilities and prepaid expense balances in each reporting period. As actual costs become known, we adjust our accrued liabilities or prepaid expenses. We have not experienced any material differences between accrued costs and actual costs incurred since our inception.

Stock-based Compensation

We measure our stock-based awards granted to employees and non-employees and shares issued under our employee stock purchase plan based on the estimated fair values of the awards on the respective grant dates. We use the Black-Scholes option-pricing model (Black-Scholes) to estimate the fair value of its stock-based awards and shares purchased under the employee stock purchase plan. The Company recognizes compensation expense for time-based awards on a straight-line basis over the requisite service period, which is generally the vesting period of the award. The Company accounts for forfeitures of stock option awards as they occur.

Black-Scholes requires the use of subjective assumptions to determine the fair value of stock-based awards.

These assumptions include:

Expected term—The expected term represents the period that stock-based awards are expected to be outstanding. The expected term for option grants is determined using the simplified method, which is the midpoint between the vesting period and the contractual term of the option.

Expected volatility—As a privately held company prior to our IPO in October 2019, we have a limited trading history for our common stock and, as such, the expected volatility is estimated based on the average volatility for comparable publicly traded biotechnology companies over a period equal to the expected term of the stock-based awards. The comparable companies were chosen based on their similar size, stage in the life cycle or area of specialty. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

Risk-free interest rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of a stock-based award.

Expected dividend—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

We will continue to use judgment in evaluating the assumptions utilized for our stock-based compensation expense calculations on a prospective basis. In addition to the assumptions used in Black-Scholes, the amount of stock-based compensation expense we recognize in our financial statements includes stock option forfeitures as they occur.

Emerging Growth Company Status

We are an emerging growth company, as defined in the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. Section 107 of the JOBS Act provides that an emerging growth company may take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933 for complying with new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. Section 107 of the JOBS Act provides that we can elect to opt out of the extended transition period at any time, which election is irrevocable. We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

Subject to certain conditions, as an emerging growth company, we may rely on certain other exemptions and reduced reporting requirements, including without limitation (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the consolidated financial statements, known as the auditor discussion and analysis. We will remain an emerging growth company until the earlier of (a) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (b) the last day of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (c) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (d) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

Recently Issued Accounting Pronouncements Not Yet Adopted

In February 2016, the Financial Accounting Standards Board, or the FASB, issued ASU 2016-02, *Leases* (Topic 842), with guidance regarding the accounting for and disclosure of leases. The update requires lessees to recognize the liabilities related all leases, including operating leases, with a term greater than 12 months on the balance sheet. This update also requires lessees and lessors to disclose key information about their leasing transactions. This guidance was effective for public companies for annual and interim periods beginning after December 15, 2018. For all other entities, including Emerging Growth Companies, this standard is effective for annual reporting periods beginning after December 15, 2020, and interim periods within annual periods beginning after December 15, 2021. Early adoption is permitted. As an Emerging Growth Company, we expect to adopt Topic 842 in 2022 and have not yet finalized the assessment of the impact that Topic 842 will have on our financial statements or financial statement disclosures.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. We held cash and cash equivalents of $122.2 million as of December 31, 2021. We generally hold our cash in interest-bearing money market treasury fund accounts. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term maturities of our cash equivalents, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents. Declines in interest rates, however, would reduce future investment income.

We do not have any foreign currency or derivative financial instruments. Inflation generally affects us by increasing our cost of labor and program costs. We do not believe that inflation had a material effect on our results of operations during the years ended December 31, 2021 and 2020.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report.An index of those financial statements is found in Item 15.

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

There has been no change of accountants nor any disagreements with accountants on any matter of accounting principles or practices of financial disclosure required to be reported under this Item.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

The Company has established disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) designed to ensure that information required to be disclosed in the reports that the Company files or submits under the Securities Exchange Act of 1934, as amended, or Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer (our Chief Executive Officer) and principal financial officer (our Chief Financial Officer), to allow timely decisions regarding required disclosure. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated, as of December 31, 2021, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) were effective at the reasonable assurance level as of December 31, 2021.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is a process designed to provide reasonable assurance of the reliability of financial reporting and of the preparation of financial statements for external reporting purposes, in accordance with U.S. generally accepted accounting principles.

Internal control over financial reporting includes policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect transactions and disposition of assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. generally accepted accounting principles, and that receipts and expenditures are being made only in accordance with the authorization of its management and directors; and (3) provide reasonable assurance regarding the prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on its financial statements.

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

Our management has assessed the effectiveness of our internal control over financial reporting as of December 31, 2021. In making this assessment, management used the criteria established by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control - Integrated Framework (2013). These criteria are in the areas of control environment, risk assessment, control activities, information and communication, and monitoring. Management's assessment included extensive documentation, evaluating and testing the design and operating effectiveness of its internal controls over financial reporting.

Based on management's processes and assessment, as described above, management has concluded that, as of December 31, 2021, our internal control over financial reporting was effective.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) that occurred during the fiscal quarter ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. As a result of the COVID-19 pandemic, since March 2020, many of our employees have been working remotely. We have not identified any material changes in our internal control over financial reporting as a result of these changes to the working environment. We are continually monitoring and assessing the COVID-19 situation to determine any potential impacts on the design and operating effectiveness of our internal controls over financial reporting.

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.

Except as set forth below, the information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2021 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2021.

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees, including our principal executive officer and principal financial officer. The Code of Business Conduct and Ethics is posted on our website at http://investors.cabalettabio.com/corporate-governance/governance-highlights.

We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of this Code of Business Conduct and Ethics by posting such information on our website, at the address and location specified above and, to the extent required by the listing standards of The Nasdaq Global Select Market, by filing a Current Report on Form 8-K with the SEC, disclosing such information.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2021 and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2021 and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2021 and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2021 and is incorporated herein by reference.

Our independent public accounting firm is Ernst & Young, Philadelphia, PA, PCAOB Auditor ID42.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this Annual Report on Form 10-K:

(1) Financial Statements:

	Page
Report of Independent Registered Public Accounting Firm	F-2
Balance Sheets as of December 31, 2021 and 2020	F-3
Statements of Operations and Comprehensive Loss for the Years Ended December 31, 2021 and 2020	F-4
Statements of Convertible Preferred Stock and Stockholders' Equity for the Years Ended December 31, 2021 and 2020	F-5
Statements of Cash Flows for the Years Ended December 31, 2021 and 2020	F-6
Notes to Financial Statements	F-7

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits. The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K. The exhibits listed in the Exhibit Index are incorporated by reference herein.

Item 16. Form 10-K Summary

None.

INDEX TO FINANCIAL STATEMENTS

	Page
Report of Independent Registered Public Accounting Firm	F-2
Balance Sheets as of December 31, 2021 and 2020	F-3
Statements of Operations and Comprehensive Loss for the Years Ended December 31, 2021 and 2020	F-4
Statements of Stockholders' Equity for the Years Ended December 31, 2021 and 2020	F-5
Statements of Cash Flows for the Years Ended December 31, 2021 and 2020	F-6
Notes to Financial Statements	F-7

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Cabaletta Bio, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Cabaletta Bio, Inc. (the Company) as of December 31, 2021 and 2020, the related statements of operations and comprehensive loss, stockholders' equity and cash flows for the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018
Philadelphia, Pennsylvania
March 17, 2022

CABALETTA BIO, INC.
Balance Sheets
(in thousands, except share and per share amounts)

	December 31,	
	2021	2020
Assets		
Current assets:		
Cash and cash equivalents	$ 122,222	$ 101,429
Short-term investments	—	7,233
Prepaid expenses and other current assets	2,319	4,873
Total current assets	124,541	113,535
Property, plant and equipment, net	1,438	890
Other assets	357	299
Total Assets	$ 126,336	$ 114,724
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,333	$ 1,243
Accrued and other current liabilities	6,047	3,937
Total current liabilities	8,380	5,180
Commitments and contingencies (see Note 7)		
Stockholders' equity:		
Preferred stock, $0.00001 par value: 10,000,000 shares authorized and no shares issued or outstanding as of December 31, 2021 and 2020	—	—
Voting and non-voting common stock, $0.00001 par value: 150,000,000 (143,590,481 voting and 6,409,519 non-voting) shares authorized as of December 31, 2021 and 2020; 28,927,129 (24,614,629 voting and 4,312,500 non-voting) shares issued and outstanding as of December 31, 2021 and 24,062,775 (19,387,160 voting and 4,675,615 non-voting) shares issued and outstanding as of December 31, 2020	—	—
Additional paid-in capital	230,543	175,836
Accumulated other comprehensive income	—	6
Accumulated deficit	(112,587)	(66,298)
Total stockholders' equity	117,956	109,544
Total liabilities and stockholders' equity	$ 126,336	$ 114,724

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

CABALETTA BIO, INC.
Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2021	**2020**
Operating expenses:		
Research and development	$ 32,494	$ 21,376
General and administrative	13,819	12,457
Total operating expenses	46,313	33,833
Loss from operations	(46,313)	(33,833)
Other income:		
Interest income	24	494
Net loss	$ (46,289)	$ (33,339)
Other comprehensive income:		
Net unrealized gain on available-for-sale investments, net of tax	$ —	$ 6
Net comprehensive loss	$ (46,289)	$ (33,333)
Net loss per voting and non-voting share, basic and diluted	$ (1.80)	$ (1.44)

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

CABALETTA BIO, INC.
Statements of Stockholders' Equity
(in thousands, except share and per share amounts)

	Common Stock					
	Shares	Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
Balance—December 31, 2019	24,034,022	$ —	$ 171,280	$ —	$ (32,959)	$ 138,321
Issuance of common stock in connection with exercise of stock options	25,611	—	139	—	—	139
Issuance of common stock under employee stock purchase plan	3,142	—	29	—	—	29
Net unrealized gains on available-for-sale securities	—	—	—	6	—	6
Stock-based compensation	—	—	4,388	—	—	4,388
Net loss	—	—	—	—	(33,339)	(33,339)
Balance—December 31, 2020	24,062,775	$ —	$ 175,836	$ 6	$ (66,298)	$ 109,544
Common stock issuance, net of $1,492 of issuance costs	4,792,562	—	48,253	—	—	48,253
Issuance of common stock in connection with exercise of stock options	64,292	—	579	—	—	579
Issuance of common stock under employee stock purchase plan	7,500	—	71	—	—	71
Net unrealized losses on available-for-sale securities	—	—	—	(6)	—	(6)
Stock-based compensation	—	—	5,804	—	—	5,804
Net loss	—	—	—	—	(46,289)	(46,289)
Balance—December 31, 2021	28,927,129	$ —	$ 230,543	$ —	$ (112,587)	$ 117,956

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

CABALETTA BIO, INC.
Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2021	**2020**
Cash flows from operating activities:		
Net loss	$ (46,289)	(33,339)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	5,804	4,388
Amortization of premium on investments	62	119
Depreciation	733	354
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	2,554	(524)
Other assets	(58)	(198)
Accounts payable	975	555
Accrued and other current liabilities	2,110	1,875
Net cash used in operating activities	(34,109)	(26,770)
Cash flows from investing activities:		
Purchases of property and equipment	(1,166)	(635)
Purchases of investments	—	(11,097)
Proceeds from maturities of investments	7,165	3,751
Net cash provided by (used in) investing activities	5,999	(7,981)
Cash flows from financing activities:		
Proceeds from issuance of common stock, net of issuance costs	48,253	(192)
Proceeds from issuance of common stock in connection with the exercise of stock options	579	139
Proceeds from the issuance of common stock under employee stock purchase plan	71	29
Net cash provided by (used in) financing activities	48,903	(24)
Net increase (decrease) in cash and cash equivalents	20,793	(34,775)
Cash and cash equivalents—beginning of year	101,429	136,204
Cash and cash equivalents—end of year	$ 122,222	$ 101,429
Supplemental disclosures of non-cash investing and financing activities:		
Property and equipment purchases included in accounts payable	$ 135	$ 20

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

1. Basis of Presentation

Cabaletta Bio, Inc. (the Company or Cabaletta) was incorporated in April 2017 in the State of Delaware as Tycho Therapeutics, Inc. and, in August 2018, changed its name to Cabaletta Bio, Inc. The Company is headquartered in Philadelphia, Pennsylvania. Cabaletta is a clinical-stage biotechnology company focused on the discovery and development of engineered T cell therapies for B cell-mediated autoimmune diseases.

Principal operations commenced in April 2018, when the Company executed two sponsored research agreements with the Trustees of the University of Pennsylvania (Penn).

On October 29, 2019, the Company completed its initial public offering (IPO) of6,800,000 shares of Common Stock at an offering price of $11.00 per share. The Company received net proceeds of $66,156 after deducting underwriting discounts, commissions and estimated offering expenses. In connection with the IPO, the Company's outstanding shares of convertible preferred stock were automatically converted into 12,904,534 shares of Common Stock. In November 2019, the underwriters partially exercised their option and purchased an additional 475,501 shares of Common Stock resulting in net proceeds to the Company of $4,864, after deducting underwriting discounts and commissions.

Risks and Uncertainties

The Company does not expect to generate revenue from sales of engineered T cell therapies for B cell-mediated autoimmune diseases or any other revenue unless and until the Company completes preclinical and clinical development and obtains regulatory approval for one or more product candidates. If the Company seeks to obtain regulatory approval for any of its product candidates, the Company expects to incur significant commercialization expenses.

The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, new technological innovations, protection of proprietary technology, dependence on key personnel, compliance with government regulations and the need to obtain additional financing. As a result, the Company is unable to predict the timing or amount of increased expenses or when or if the Company will be able to achieve or maintain profitability. Further, the Company is currently dependent on Penn for much of its preclinical research, clinical research and development activities and initial manufacturing activities (Note 6). Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization. Even if the Company is able to generate revenues from the sale of its product candidates, if approved, it may not become profitable. If the Company fails to become profitable or is unable to sustain profitability on a continuing basis, then it may be unable to continue its operations at planned levels and be forced to reduce its operations.

In December 2019, a novel strain of coronavirus (COVID-19) surfaced in Wuhan, China and has since reached multiple other regions and countries. The COVID-19 pandemic has continued to evolve as new variants of COVID-19 have been identified and spread, which has led to various responses, including government-imposed quarantines, travel restrictions and other public health safety measures in response to the emergence of new variants. The extent to which COVID-19 will continue to impact the Company's operations or those of its third party partners will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the pandemic, new information that may emerge concerning the severity of COVID-19, the impact of new strains of the virus, the effectiveness, availability and utilization of vaccines and the actions to contain COVID-19 or treat its impact, among others. The Company's financial results to date have not been significantly impacted by COVID-19, however, the Company cannot at this time predict the specific extent, duration, or full impact that the ongoing COVID-19 pandemic will have on its financial condition, operations, and business plans, including its ability to raise additional capital, the timing and enrollment of patients in its ongoing and planned clinical trials, future financings and other expected milestones of its product candidates.

Liquidity

The Company has sustained annual operating losses since inception and expects to continue to generate operating losses for the foreseeable future. The Company's ultimate success depends on the outcome of its research and development activities. The Company had cash and cash equivalents of $122,222 as of December 31, 2021. Through December 31, 2021, the Company has incurred an accumulated deficit of $112,587. Management expects to incur additional losses in the future as it continues its research and development and will need to raise additional capital to fully implement its business plan and to fund its operations.

The Company intends to raise such additional capital through a combination of equity offerings, debt financings, government funding arrangements, strategic alliances or other sources. However, if such financing is not available at adequate levels and on a timely basis, or such agreements are not available on favorable terms, or at all, as and when needed, the Company will need to reevaluate its operating plan and may be required to delay or discontinue the development of one or more of its product candidates or operational initiatives. The Company expects that its cash and cash equivalents as of December 31, 2021 will be sufficient to fund its projected operations for at least 12 months following the date the Company files this Annual Report on Form 10-K with the Securities and Exchange Commission (SEC).

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America (GAAP) requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the financial statements and the reported amounts of expenses during the reporting period. Significant estimates and assumptions made in the accompanying financial statements include but are not limited to the fair value of stock-based compensation, the valuation allowance on the Company's deferred tax assets and certain accruals. The Company evaluates its estimates and assumptions on an ongoing basis using historical experience and other factors and adjusts those estimates and assumptions when facts and circumstances dictate. Actual results could differ from those estimates.

Off-Balance Sheet Risk and Concentrations of Credit Risk

Financial instruments, which potentially subject the Company to significant concentrations of credit risk, consist of cash and cash equivalents, which are primarily invested in U.S. treasury-based money market funds. As of December 31, 2020, the Company held available-for-sale debt securities, which were invested in investment grade corporate bonds with high credit quality issuers. These investments matured in 2021. A portion of the Company's cash is maintained at a federally insured financial institution. The deposits held at this institution are in excess of federally insured limits. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institution in which those deposits are held. The cash in this account is swept daily into U.S. treasury-based and U.S. government-based money market funds. The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements.

Cash and Cash Equivalents

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

Investments

Investments are available-for-sale and carried at estimated fair value. The Company's valuations of available-for-sale debt securities are generally derived from independent pricing services based upon quoted prices in active markets for similar securities, with prices adjusted for yield and number of days to maturity, or based on industry models using data inputs, such as interest rates and prices that can be directly observed or corroborated in active

markets. Management determines the appropriate classification of its investments in debt securities at the time of purchase and at the end of each reporting period. Investments with original maturities beyond three months at the date of purchase and which mature at, or less than, twelve months from the balance sheet date are classified as current.

Unrealized gains and losses are excluded from earnings and are reported as a component of comprehensive income. The Company periodically evaluates whether declines in fair values of its available-for-sale securities below their book value are other-than-temporary. This evaluation consists of several qualitative and quantitative factors including the severity and duration of the unrealized loss as well as the Company's ability and intent to hold the available-for-sale security until a forecasted recovery occurs. Additionally, the Company assesses whether it has plans to sell the security or if more likely than not it will be required to sell any available-for-sale securities before recovery of its amortized cost basis. Realized gains and losses and declines in fair value judged to be other-than-temporary, if any, on available-for-sale securities are included in interest and other income, net. The cost of investments sold is based on the specific-identification method. Interest income on investments as well as amortization of discount or premium is included in interest income.

Property, Plant and Equipment

Property, plant and equipment are recorded at cost less accumulated depreciation. Cost includes the acquisition costs and all costs necessary to bring the asset to the location and working condition necessary for its intended use. Depreciation expense is recognized using the straight-line method over the estimated useful life of each asset. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in the accompanying statements of operations. Expenditures for normal, recurring or periodic repairs and maintenance related to property and equipment are charged to expense as incurred. The cost for planned major maintenance activities, including the related acquisition or construction of assets, is capitalized if it will result in future economic benefits.

Estimated useful lives for property and equipment are as follows:

Property and equipment	Estimated useful life
Laboratory equipment	Three years
Furniture and fixtures	Three years
Computer equipment	Three years
Leasehold improvements	Lesser of estimated useful life or remaining lease term

Fair Value Measurement

Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Observable inputs such as unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2—Inputs (other than quoted prices included in Level 1) that are either directly or indirectly observable for the asset or liability. These include quoted prices for similar assets or liabilities in active markets and quoted prices for identical or similar assets or liabilities in markets that are not active.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Research and Development Expenses

Research and development costs include costs incurred for internal and external research and development activities and are expensed as incurred in the accompanying statements of operations. Research and development costs consist of salaries and benefits, including associated stock-based compensation, and laboratory supplies and facility costs, as well as fees paid to entities that conduct certain research and development activities on the Company's behalf.

The Company records accrued liabilities for estimated costs of research and development activities conducted by service providers, which include activities under agreements with Penn (Note 6), the conduct of sponsored research, preclinical studies and contract manufacturing activities. The Company records the estimated costs of research and development activities based upon the estimated amount of services provided and includes these costs in accrued and other current liabilities and prepaid expenses and other current assets in the accompanying balance sheets and within research and development expense in the accompanying statements of operations. Non-refundable advance payments made for goods or services that will be used or rendered for future research and development activities are deferred and capitalized and recognized as expense as the goods are received or the related services are rendered.

The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with service providers. The Company makes significant judgments and estimates in determining the accrued liabilities and prepaid expenses in each reporting period. As actual costs become known, the Company adjusts its accrued liabilities and prepaid expenses. The Company has not experienced any material differences between accrued costs and actual costs incurred since its inception.

Stock-based Compensation

The Company measures its stock-based awards granted to employees and non-employees based on the estimated fair values of the awards on the respective grant dates. The Company uses the Black-Scholes option-pricing model (Black-Scholes) to estimate the fair value of its stock-based awards. The Company recognizes compensation expense for time-based awards on a straight-line basis over the requisite service period, which is generally the vesting period of the award. The Company accounts for forfeitures of stock option awards as they occur.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes. Deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to temporary differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax base. Deferred tax assets and liabilities, which relate primarily to the carrying amount of the Company's property and equipment and its net operating loss carryforwards, are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. Deferred tax expense or benefit is the result of changes in the deferred tax assets and liabilities. Valuation allowances are established when necessary to reduce deferred tax assets where, based upon the available evidence, the Company concludes that it is more-likely-than-not that the deferred tax assets will not be realized. In evaluating its ability to recover deferred tax assets, the Company considers all available positive and negative evidence, including its operating results, ongoing tax planning and forecasts of future taxable income on a jurisdiction-by-jurisdiction basis. Because of the uncertainty of the realization of deferred tax assets, the Company has recorded a full valuation allowance against its deferred tax assets.

Reserves are provided for tax benefits for which realization is uncertain. Such benefits are only recognized when the underlying tax position is considered more-likely-than-not to be sustained on examination by a taxing authority, assuming they possess full knowledge of the position and facts. Interest and penalties related to uncertain tax positions are recognized in the provision of income taxes; however, the Company currently has no interest or penalties related to uncertain income tax benefits.

Net Loss Per Share

The Company calculates basic and diluted net loss per share attributable to common stockholders in conformity with the two-class method required for participating securities. The Company has voting and non-voting common stock. The rights, including the liquidation and dividend rights, of the holders of the voting and non-voting common stock are identical, except with respect to voting. Each share of non-voting common stock may be converted at any

time into one share of voting common stock at the option of its holder by providing written notice to the Company, subject to the limitations provided for in the amended and restated certificate of incorporation. The Company also considers its unvested shares of common stock held by the Company's foundersand, prior to its conversion to common stock, its convertible preferred stock to be participating securities as, in the event a dividend is paid on common stock, the holders of convertible preferred stock and unvested shares of common stock would be entitled to receive dividends on a basis consistent with the common stockholders.

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock, which excludes unvested shares of common stock. The undistributed loss for each year is allocated to common stockholders based on the contractual participation rights of the voting and non-voting common stock as if the losses for the year had been distributed. As the liquidation and dividend rights are identical, the undistributed losses are allocated on a proportionate basis. Diluted net loss per share attributable to common stockholders is computed under the if-converted method and assumes that all non-voting common stock has been converted to common stock. Since the Company was in a loss position for all periods presented, the effects of the other potentially dilutive securities are antidilutive.

Segments

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the Chief Operating Decision Maker (CODM) in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is its Chief Executive Officer. The Company has determined it operates in a single operating segment and has one reportable segment.

Emerging Growth Company Status

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act, until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (i) is no longer an emerging growth company or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, these financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

Recently Issued Accounting Pronouncements Not Yet Adopted

In February 2016, the Financial Accounting Standards Board (FASB) issued ASU 2016-02, *Leases* (Topic 842), with guidance regarding the accounting for and disclosure of leases. The update requires lessees to recognize the liabilities related all leases, including operating leases, with a term greater than 12 months on the balance sheet. This update also requires lessees and lessors to disclose key information about their leasing transactions. This guidance will be effective for public companies for annual and interim periods beginning after December 15, 2018. For all other entities, including Emerging Growth Companies, this standard is effective for annual reporting periods beginning after December 15, 2020, and interim periods within annual periods beginning after December 15, 2021. Early adoption is permitted. As an Emerging Growth Company, the Company expects to adopt Topic 842 in 2022 and has not yet finalized the assessment of the impact that Topic 842 will have on its financial statements or financial statement disclosures.

3. Fair Value Measurements

As of December 31, 2021 and 2020, the Company's financial instruments included cash and cash equivalents, accounts payable and accrued expenses. As of December 31, 2020, the Company also had available-for-sale debt securities. The carrying amounts for cash and cash equivalents, accounts payable and accrued expenses reported in

the Company's financial statements for these instruments approximate their respective fair values because of the short-term nature of these instruments.

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

	December 31, 2021			
	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Financial assets				
Cash and cash equivalents:				
Money market funds	$ 122,222	$ 122,222	$ —	$ —
Total	$ 122,222	$ 122,222	$ —	$ —

	December 31, 2020			
	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Financial assets				
Cash and cash equivalents:				
Money market funds	$ 101,429	$ 101,429	$ —	$ —
Short-term investments:				
Corporate bonds	7,233	—	7,233	—
Total	$ 108,662	$ 101,429	$ 7,233	$ —

Money market funds are measured at fair value on a recurring basis using quoted prices and are classified as Level 1. Investments are measured at fair value based on inputs other than quoted prices that are derived from observable market data and are classified as Level 2 inputs.

For debt securities classified as available-for-sale investments, the Company records unrealized gains or losses resulting from changes in fair value between measurement dates as a component of other comprehensive income. The Company did not hold any available-for-sale securities as of December 31, 2021.

	December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair value
Financial assets				
Money market funds				
Included in cash and cash equivalents	$ 101,429	$ —	$ —	$ 101,429
Corporate bonds - due in one year or less				
Included in short-term investments	7,227	6	—	7,233
Total	$ 108,656	$ 6	$ —	$ 108,662

4. Property, Plant and Equipment

Property plant and equipment consists of the following:

	December 31,	
	2021	2020
Laboratory equipment	$ 2,242	$ 961
Furniture and fixtures	277	277
Leasehold improvements	57	57
Computer equipment	53	53
Total property, plant and equipment	2,629	1,348
Less: accumulated depreciation	(1,191)	(458)
Property, plant and equipment, net	$ 1,438	$ 890

Depreciation expense was $733 and $354 for the years ended December 31, 2021 and 2020, respectively.

5. Accrued and Other Current Liabilities

Accrued and other current liabilities consist of the following:

	December 31,	
	2021	2020
Research and development services	$ 2,836	$ 1,294
General and administrative services	180	160
Compensation expense	2,977	2,445
Other	54	38
	$ 6,047	$ 3,937

6. Collaborations, Licensing Agreements and other Agreements

Amended and Restated License Agreement with the Trustees of the University of Pennsylvania and Children's Hospital of Philadelphia

In August 2018, the Company entered into a license agreement with Penn, as amended and restated in July 2019 to include the Children's Hospital of Philadelphia (CHOP) as a party, and as amended in May 2020 and October 2021 (the License Agreement) pursuant to which the Company obtained (a) a non-exclusive, non-sublicensable worldwide license to certain of Penn's intellectual property to conduct research, product development, clinical trials, cell manufacturing and other activities, and (b) an exclusive, worldwide, royalty-bearing right and license, with a right to sublicense, on a target-by-target basis, under certain of Penn's intellectual property to make, use, sell, offer for sale, import, and otherwise commercialize products for the treatment of autoimmune and alloimmune diseases.

Unless earlier terminated, the License Agreement expires on the expiration or abandonment or other termination of the last valid claim in Penn's intellectual property licensed by the Company. The Company may terminate the License Agreement at any time for convenience upon 60 days written notice. In the event of an uncured, material breach, Penn may terminate the License Agreement upon 60 days written notice.

Under the terms of the License Agreement, the Company was obligated to pay $2,000 annually for three years beginning August 2018 for funding to the laboratories of each of Drs. Milone and Payne (see *Sponsored Research Agreements*). During the term of the License Agreement until the first commercial sale of the first product, the Company is obligated to pay Penn a non-refundable, non-creditable annual license maintenance fee of $10. In May 2020, the Company paid Penn an additional, non-refundable, non-creditable license fee of $33 under the amended License Agreement.

The Company is required to pay certain milestone payments upon the achievement of specified clinical and commercial milestones. Milestone payments are reduced by a certain percentage for the second product that achieves

a milestone, by an additional percentage for the third product that achieves a milestone, and so on, for each subsequent product that achieves a milestone. In the event that the Company is able to successfully develop and launch multiple products under the License Agreement, total milestone payments could be approximately $21,000. Penn is also eligible to receive tiered royalties at percentage rates in the low single-digits, subject to an annual minimum royalty, on annual worldwide net sales of any products that are commercialized by the Company or its sublicensees that contain or incorporate, or are covered by, the intellectual property licensed by the Company. To the extent the Company sublicenses its license rights under the License Agreement, Penn would be eligible to receive tiered sublicense income at percentage rates in the mid-single to low double-digits. There were no amounts due under the License Agreement as of December 31, 2021 or 2020.

Sponsored Research Agreements

The Company has sponsored research agreements, or SRA, with two faculty members at Penn, who are also scientific co-founders of the Company and members of the Company's scientific advisory board. In May 2020, one of the SRAs was amended to expand the scope of sponsored research. In August 2020, the same SRA was further amended to extend the term of the original research plan. In December 2021, the Company further amended this SRA to extend the term and expand the workplan to include additional correlative studies related to the DesCAARTes™ trial. In April 2021 and October 2021, the other SRA was amended to extend the term of the original research plan.

Under the amended SRAs, the Company has committed to funding defined research plans through December 2024 and November 2022, respectively. The total estimated cost of $12,483 under the SRAs satisfies the Company's annual obligation under the License Agreement (see *Amended and Restated License Agreement with the Trustees of the University of Pennsylvania* above). As of December 31, 2021, $9,930 of cost has been incurred pursuant to these SRAs. For the years ended December 31, 2021 and 2020, the Company recognized research and development expense of $2,840 and $2,995, respectively, related to these SRAs in the accompanying statements of operations. As of December 31, 2021 and 2020, $346 and $1,851 respectively, of advance payments are included in Prepaid expenses and other current assets in the accompanying balance sheets and there was $36 and $217 included in Accrued and other current liabilities in the accompanying balance sheets as of December 31, 2021 and 2020.

In December 2021, the Company entered into a SRA with Penn for the laboratory of Dr. Drew Weissman, or the Weissman SRA. Under the Weissman SRA, discovery-stage proof of concept studies for lipid nanoparticle mRNA for the delivery and/or enhancement of CAAR technology is being conducted. Under the Weissman SRA, Penn granted the Company a non-transferable, non-exclusive license to use certain intellectual property for specific internal research purposes and further grants the Company the first option to negotiate to acquire, subject to agreement on commercial terms, an exclusive or non-exclusive worldwide license to certain patent rights for specific CAAR products developed under the Weissman SRA. Unless earlier terminated, the Weissman SRA will expire in December 2023. Pursuant to the Weissman SRA, the Company also entered into an Option Agreement with Penn, or the Weissman Option, which grants the Company the option to negotiate to acquire a non-exclusive worldwide license to certain patent rights in connection with the Weissman SRA.

Master Translational Research Services Agreement

In October 2018, the Company entered into a services agreement (the Services Agreement) with Penn for additional research and development services from various laboratories within Penn. The research and development activities are detailed in separately executed Penn organization-specific addenda. In May 2020, the Company amended its Addendum with the Center for Advanced Retinal and Ocular Therapeutics (CAROT) to expand access to vector manufacturing.

Research and development expense related to executed addenda under the master translational research service agreement with Penn recognized in the accompanying statements of operations for the years ended December 31, 2021 and 2020 was $1,933 and $2,474, respectively. The Company may incur additional expenses up to $1,360 through the remaining term of the CAROT Amended Addendum.

Subscription and Technology Transfer Agreement

In July 2019, the Company entered into a subscription and technology transfer agreement pursuant to which the Company owed Penn an upfront subscription fee, which was paid in 2019, and a nominal non-refundable royalty on the net sales of products, a portion of which will be credited toward milestone payments and royalties, respectively, under the Amended License Agreement. Technology transfer activities will be at the Company's cost and subject to agreement as to the technology to be transferred. The Company recognized $150 of research and development expense under this agreement for the year ended December 31, 2021.No expense was recognized under this agreement for the year ended December 31, 2020.

Artisan Collaboration and License Agreement

In July 2020, the Company entered into a collaboration and license agreement with Artisan Bio, Inc. (Artisan), wherein the Company and Artisan agreed to collaborate to potentially enhance certain pipeline products of the Company at specific targets using Artisan's gene editing and engineering technology. If the Artisan technology is applied to any of the Company's products, the Company will be responsible for the development, manufacturing, and commercialization of any such products. Under the terms of the agreement, the Company was required to pay Artisan a nominal upfront fee, as well as costs associated with research and development activities. Artisan is eligible to receive future research, development and regulatory milestones, and is also eligible to receive sales milestones and tiered royalties on net sales of products that incorporate the Artisan technology. The Company can terminate the agreement at will upon advance written notice with payment of a nominal cancellation fee.

Licence and Supply Agreement with Oxford Biomedica

In December 2021, the Company entered into a Licence and Supply agreement (LSA) with Oxford Biomedica (UK) Limited, wherein the LSA grants the Company a non-exclusive license to Oxford's LentiVector® platform for its application in the Company's DSG3-CAART program and puts in place a multi-year vector supply agreement. Under the terms of the agreement, the Company is required to pay Oxford an upfront fee, as well as costs associated with initial vector manufacturing activities for a total cost of up to approximately $4,000. Oxford is eligible to receive regulatory and sales milestones in the low tens of millions and royalties in the low single digits on net sales of products that incorporate the Oxford technology. The Company can terminate the agreement at will upon advance written notice and subject to certain manufacturing slot cancellation fees. As of December 31, 2021, the Company has recognized expenses of approximately $1,100 in the accompanying statements of operations under this LSA.

7. Commitments and Contingencies

Operating Lease Agreement

In February 2019, the Company entered into an operating lease agreement for new office space in Philadelphia, Pennsylvania.The lease term commenced in May 2019 and will expire in July 2022. The initial annual base rent is $261, and such amount will increase by 2% annually on each anniversary of the commencement date. The Company records rent expense on a straight-line basis over the lease term. Rent expense related to this lease agreement recognized in the accompanying statement of operations was $272 and $266 for the years ended December 31, 2021 and 2020. In February 2022, the Company amended this lease for an additional 5 months, through June 30, 2025. The annual base rent is $279, starting on January 1, 2023 and such amount will increase by 2.5% annually.

In January 2021, the Company entered into a Development and Manufacturing Services Agreement (WuXi Agreement) with WuXi Advanced Therapies, Inc. (WuXi) to serve as the Company's cell processing manufacturing partner for the planned MuSK-CAART Phase 1 clinical trial, or MusCAARTes ™ trial. The Company concluded the WuXi Agreement has an embedded lease as a dedicated manufacturing suite is used for the Company's cell processing manufacturing. The monthly fee of $ 125 for this suite is included in the minimum lease payment table below. During the year ended December 31, 2021, the Company recognized $ 480 of expense related to this lease in the accompanying statements of operations. The WuXi Agreement will expire the later of January 2024, or upon completion of WuXi's services related to the MusCAARTes™ trial. The Company has the right to terminate the WuXi Agreement for convenience or other reasons specified in the WuXi Agreement upon prior written notice. If the Company terminates the WuXi Agreement, it will be obligated to pay an early termination fee of up to $1,500.

As of December 31, 2021, the future minimum payments for operating leases are as follows:

2022	$	1,658
2023		1,500
2024		1,500
Thereafter		—
	$	4,658

Research Service Agreement

In February 2021, the Company entered into a research service agreement with CHOP for vector manufacturing. In May 2021, this agreement was amended to provide additional vector manufacturing services. Research and development expense related to this research service agreement with CHOP recognized in the accompanying statements of operations was $1,071 for the year ended December 31, 2021. No expense was recognized for the year ended December 31, 2020. There was $166 recorded in Accrued and other current liabilities in the accompanying balance sheets as of December 31, 2021. This agreement has a remaining cost of approximately $646, expected to be incurred through the first half of 2023.

Manufacturing Agreement

In August and October 2021, the Company entered into agreements with a contract manufacturing organization for the purchase of plasmids to be used in vector manufacturing for a total cost of approximately $1,620, expected to be incurred during 2021 and 2022. As of December 31, 2021, $1,310 of expense related to these agreements has been recognized in the accompanying statements of operations. There was $827 recorded in Accrued and other current liabilities in the accompanying balance sheets as of December 31, 2021.

Other Purchase Commitments

In the normal course of business, the Company enters into various purchase commitments with third-party contract manufacturers for the manufacture and processing of its product candidates and related raw materials, contracts with contract research organizations for clinical trials and agreements with vendors for other services and products for operating purposes. These agreements generally provide for termination or cancellation, other than for costs already incurred.

Indemnification

The Company enters into certain types of contracts that contingently requires the Company to indemnify various parties against claims from third parties. These contracts primarily relate to (i) the Company's bylaws, under which the Company must indemnify directors and executive officers, and may indemnify other officers and employees, for liabilities arising out of their relationship, (ii) contracts under which the Company must indemnify directors and certain officers and consultants for liabilities arising out of their relationship, (iii) contracts under which the Company may be required to indemnify partners against certain claims, including claims from third parties asserting, among other things, infringement of their intellectual property rights, and (iv) procurement, consulting, or license agreements under which the Company may be required to indemnify vendors, consultants or licensors for certain claims, including claims that may be brought against them arising from the Company's acts or omissions with respect to the supplied products, technology or services. From time to time, the Company may receive indemnification claims under these contracts in the normal course of business. In addition, under these contracts, the Company may have to modify the accused infringing intellectual property and/or refund amounts received.

In the event that one or more of these matters were to result in a claim against the Company, an adverse outcome, including a judgment or settlement, may cause a material adverse effect on the Company's future business, operating results or financial condition. It is not possible to determine the maximum potential amount under these contracts due to the limited history of prior indemnification claims and the unique facts and circumstances involved in each particular agreement.

Pending Litigation

On February 28, 2022, a purported stockholder of the Company filed a complaint against the Company and certain of the Company's current officers and certain of the Company's current and former directors in the United States District Court for the Eastern District of Pennsylvania captioned *Patterson v. Cabaletta Bio, Inc., et al*.. No. 2:22-cv-00737 (E.D. Pa.). The complaint was filed on behalf of a putative class of persons and entities who purchased or otherwise acquired (a) Cabaletta common stock pursuant and/or traceable to the offering documents issued in connection with the Company's October 24, 2019 initial public offering; and/or (b) Cabaletta securities between October 24, 2019 and December 13, 2021 both dates inclusive. The complaint alleges claims under Sections 10(b) and 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder and under Sections 11 and 15 of the Securities Act based upon allegedly false or misleading statements and omissions regarding our DesCAARTes ™ Phase 1 clinical trial of DSG3-CAART, clinical data for the DesCAARTes™ trial, the efficacy of DSG3-CAART, and the clinical and/or commercial prospects for DSG3-CAART. The complaint seeks damages, prejudgment and post-judgment interest, and reasonable attorneys' fees, expert fees and other costs. The Company may also become subject to additional securities class action lawsuits in the future. The Company intends to vigorously defend the lawsuit. At this time, no assessment can be made as to its likely outcome or whether the outcome will be material to the Company. No information is available to indicate that it is probable that a loss has been incurred and can be reasonably estimated as of the date of the financial statements and, as such, no accrual for the loss has been recorded within the financial statements.

8. Common Stock

Common Stock

Pursuant to the Company's Third Amended and Restated Certificate of Incorporation filed in October 2019, the Company is authorized to issue 143,590,481 shares of voting common stock and 6,409,519 shares of non-voting common stock. Holders of voting commonstock shall have the exclusive right to vote for the election of directors of the Company and on all other matters requiring stockholder action. Each share of the Company's non-voting common stock may be converted at any time into one share of common stock at the option of its holder by providing written notice to the Company, subject to the limitations provided for in the amended and restated certificate of incorporation.

The Company has a Sales Agreement with Cowen and Company, LLC, to provide for the offering, issuance and sale of up to an aggregate amount of $75.0 million of common stock from time to time in "at-the-market" offerings (the ATM Program) pursuant to its shelf registration statement on Form S-3 (File No. 333-250006) and subject to the limitations thereof. During the year ended December 31, 2021, the Company sold 4,792,562 shares pursuant to the ATM Program for net proceeds of $48.3 million, after deducting commissions of $1.4 million.

2018 Stock Option and Grant Plan

In September 2018, the Company adopted the 2018 stock option and grant plan (the 2018 Plan), which provided for the Company to sell or issue common stock, or other stock-based awards, to employees, members of the board of directors and consultants of the Company. The Company generally granted stock-based awards with service conditions only (service-based awards), although there was one grant with performance conditions. As of December 31, 2020, there are no unvested options with performance conditions. Stock options granted under the 2018 Plan generally vest over three to four years. There were 1,959,411 options granted under the 2018 Plan prior to the Company's IPO in October 2019. No further grants may be made under the 2018 Plan subsequent to the IPO.

2019 Stock Option and Incentive Plan

The 2019 Stock Option and Incentive Plan (2019 Plan) was approved by the Company's board of directors on October 14, 2019, and became effective on October 23, 2019. The 2019 Plan provides for the grant of incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock units, restricted stock awards, unrestricted stock awards, cash-based awards and dividend equivalent rights to the Company's officers, employees, directors and consultants. The number of shares initially reserved for issuance under the 2019 Plan was 2,342,288, which will be increased each January 1 thereafter by 4% of the number of shares of the Company's common stock outstanding on the immediately preceding December 31 or such lesser number of shares determined by the Company's board of directors or compensation committee of the board of directors. On January 1, 2022, the total number of shares under the 2019 Plan was increased by 1,157,085 shares. As of December 31, 2021, there were 1,855,788 shares remaining available for issuance.

A summary of the stock option activity is presented below:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value
Outstanding as of January 1, 2021	2,900,479	$ 7.33	8.5	16,303
Granted	1,653,733	10.87		
Exercised	(64,292)	9.00		102
Forfeited/Cancelled	(232,707)	10.87		
Outstanding as of December 31, 2021	4,257,213	$ 8.49	8.2	$ 2,367
Options Exercisable at December 31, 2021	1,751,754	$ 5.89	7.3	$ 2,028

The aggregate intrinsic value of options granted is calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock. The weighted average grant-date fair value of stock options granted during the year ended December 31, 2021 and 2020 was $7.45 and $8.31, respectively.

The fair value of each award is estimated using Black-Scholes based on the following assumptions:

	For the Year Ended December 31,	
	2021	2020
Risk-free interest rate	0.63%—1.39%	0.28%—1.48%
Expected term	5.5—6.1 years	5.7—6.1 years
Expected volatility	79%—81%	70%—79%
Expected dividend yield	0%	0%

Black-Scholes requires the use of subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

Expected term—The expected term represents the period that stock-based awards are expected to be outstanding. The expected term for option grants is determined using the simplified method, which is the midpoint between the vesting period and the contractual term of the option.

Expected volatility—As a privately held company prior to the Company's IPO in October 2019, the Company has limited trading history for its common stock and, as such, the expected volatility is estimated based on the average volatility for comparable publicly traded biotechnology companies over a period equal to the expected term of the stock-based awards. The comparable companies were chosen based on their similar size, stage in the life cycle or area of specialty. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Risk-free interest rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of a stock-based award.

Expected dividend—The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

Stock-based Compensation

The Company has recorded stock-based compensation in the accompanying statements of operations as follows:

	For the Year Ended December 31,	
	2021	2020
Research and development	$ 2,746	$ 1,989
General and administrative	3,058	2,399
Total	$ 5,804	$ 4,388

As of December 31, 2021, there was $14,897 of unrecognized compensation cost related to unvested option awards,which is expected to be recognized over a weighted-average period of 2.6 years.

2019 Employee Stock Purchase Plan

The 2019 Employee Stock Purchase Plan (2019 ESPP) was approved by the Company's board of directors on October 14, 2019, and became effective on October 23, 2019. A total of 234,229 shares of common stock were initially reserved for issuance under the 2019 ESPP, and will be increased each January 1 thereafter through January 1, 2029 by the least of (i) 234,229 shares of common stock, (ii) 1% of the number of shares of the Company's common stock outstanding on the immediately preceding December 31 or (iii) such lesser number of shares determined by the 2019 ESPP's administrator. On January 1, 2022, there was no increase to the total number of shares under the 2019 ESPP.

Employee contributions are made through payroll deductions of up to 15% of eligible compensation over the offering period. A participant may not accrue rights to purchase more than $25 worth of the Company's common stock for each calendar year in which such right is outstanding. At the end of each offering period, shares of the Company's common stock may be purchased at 85% of the lesser of the Company's common stock on (i) the first trading day of the relevant offering period and (ii) the last trading day of the relevant offering period. The first offering period commenced on July 1, 2020 and ended on November 30, 2020. Thereafter, offerings will be six months in duration and will commence on each December 1 and June 1.

9. Income Taxes

The reconciliation of federal statutory income tax rate to the Company's effective income tax rate is as follows:

	For the Year Ended December 31,	
	2021	2020
Expected income tax benefit at the federal statutory rate	21.0 %	21.0 %
State and local taxes, net of federal benefit	12.5	12.5
Research and development credit, net	4.4	2.6
Non-deductible items and other	(0.6)	(0.8)
Change in valuation allowance	(37.3)	(35.3)
Total	0.0 %	0.0 %

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The principal components of the Company's deferred tax assets consisted of the following:

	December 31,	
	2021	2020
Deferred tax assets:		
Federal, state and local net operating loss carryforwards	$ 28,857	$ 15,241
License fee deductions	318	340
Research and development tax credits	3,359	1,317
Stock-based compensation deductions	2,616	1,243
Accrued expenses	1,074	837
Gross deferred tax assets	36,224	18,978
Less: valuation allowance	(36,224)	(18,978)
Total deferred tax assets	—	—
Deferred tax liabilities:	—	—
	$ —	$ —
Net deferred tax assets	$ —	$ —

The Company increased its valuation allowance by $17,246 for the year ended December 31, 2021 in order to maintain a full valuation allowance against its deferred tax assets. Based on the Company's history of losses, the Company recorded a full valuation allowance against its deferred tax assets as of December 31, 2021. The Company intends to maintain a valuation allowance until sufficient positive evidence exists to support a reversal of the allowance.

As of December 31, 2021, the Company had federal, state and local net operating loss carryforwards of $85,798, $87,983 and $78,892, respectively; $85,548 of the federal amounts do not expire, and the remaining $250 expire in 2037. The state net operating losses begin to expire in 2037. The local net operating losses begin to expire in 2039. As of December 31, 2021, the Company had federal research and development tax credit carryforwards of $3,359, which begin to expire in 2038. Under the provisions of Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the IRC), these net operating losses, credit carryforwards and other tax attributes may be subject to limitation based on previous significant changes in ownership and upon future significant changes in ownership of the Company, as defined by the IRC.

The Company files income tax returns in the U.S. federal jurisdiction as well as in Pennsylvania and Philadelphia. The tax years 2020, 2019 and 2018 remain open to examination by the jurisdictions where the Company is subject to tax.

The Company evaluates tax positions for recognition using a more-likely-than-not recognition threshold, and those tax positions eligible for recognition are measured as the largest amount of tax benefit that is greater than 50% likely of being realized upon the effective settlement with a taxing authority that has full knowledge of all relevant information. As of December 31, 2021, the Company had no unrecognized income tax benefits that would affect the Company's effective tax rate if recognized.

10. Net Loss Per Share

The Company calculates basic and diluted net loss per share attributable to common stockholders in conformity with the two-class method required for participating securities. For the years ended December 31, 2021 and 2020, the Company had voting and non-voting common stock outstanding. Since the rights of the voting and non-voting common stock are identical, except with respect to voting, the undistributed losses of the Company have been allocated on a proportionate basis to the two classes. Diluted net loss per share is calculated using the if-converted method, which assumes conversion of all non-voting common stock to voting common stock.

	Year ended December 31, 2021	
	Voting common stock	Non-voting common stock
Basic net loss per share:		
Numerator		
Allocation of undistributed losses attributable to common stockholders	$ (38,417)	$ (7,872)
Denominator		
Weighted average number of shares used in basic per share computation	21,360,544	4,376,776
Net loss per share, basic	$ (1.80)	$ (1.80)
Diluted net loss per share:		
Numerator		
Allocation of undistributed losses for basic computation	$ (38,417)	$ (7,872)
Reallocation of undistributed losses as a result of conversion of non-voting to voting common shares	(7,872)	—
Allocation of undistributed losses	$ (46,289)	$ (7,872)
Denominator		
Weighted average number of shares used in basic per share computation	21,360,544	4,376,776
Add: Conversion of non-voting to voting common shares outstanding	4,376,776	—
Weighted average number of shares used in diluted per share computation	25,737,320	4,376,776
Net loss per share, diluted	$ (1.80)	$ (1.80)

	Year ended December 31, 2020	
	Voting common stock	Non-voting common stock
Basic net loss per share:		
Numerator		
Allocation of undistributed losses attributable to common stockholders	$ (25,090)	$ (8,249)
Denominator		
Weighted average number of shares used in basic per share computation	17,417,900	5,727,327
Net loss per share, basic	$ (1.44)	$ (1.44)
Diluted net loss per share:		
Numerator		
Allocation of undistributed losses for basic computation	$ (25,090)	$ (8,249)
Reallocation of undistributed losses as a result of conversion of non-voting to voting common shares	(8,249)	—
Allocation of undistributed losses	$ (33,339)	$ (8,249)
Denominator		
Weighted average number of shares used in basic per share computation	17,417,900	5,727,327
Add: Conversion of non-voting to voting common shares outstanding	5,727,327	—
Weighted average number of shares used in diluted per share computation	23,145,227	5,727,327
Net loss per share, diluted	$ (1.44)	$ (1.44)

The following outstanding potentially dilutive shares have been excluded from the calculation of diluted net loss per share, as their effect is anti-dilutive:

	For the Year Ended December 31,	
	2021	2020
Stock options to purchase common stock	4,257,213	2,900,479
Non-vested founder stock	—	465,801
Total	4,257,213	3,366,280

11. 401(k) Savings Plan

The Company maintains a defined-contribution savings plan under Section 401(k) of the IRC, or the 401(k) Plan. The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pretax basis. In 2019, the Company made a safe harbor nonelective contribution of 3% of eligible compensation on behalf of all employees. Effective January 1, 2020, the Plan provided for matching contributions on a portion of participant contributions pursuant to the 401(k) Savings Plan's matching formula, up to 4% of eligible compensation. All matching contributions and participant contributions vest immediately. Contributions totaled $256 and $203 for the years ended December 31, 2021 and 2020, respectively, and have been recorded in the statements of operations.

EXHIBIT INDEX

Exhibit Number	Description
3.1	Third Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect (incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K (File No. 001-39103) filed on October 30, 2019)
3.2	Amended and Restated Bylaws of the Registrant, as currently in effect (incorporated by reference to Exhibit 3.2 of the Registrant's Current Report on Form 8-K (File No. 001-39103) filed on October 30, 2019)
4.1	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-234017) filed on October 16, 2019)
4.2	Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, dated January 2, 2019 (incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-234017) filed on September 30, 2019)
4.3	Description of Securities (incorporated by reference to Exhibit 4.3 of the Registrant's Annual Report on Form 10-K (File No. 001-39103) filed on March 30, 2020)
10.1#	2018 Stock Option and Grant Plan, as amended, and form of award agreements thereunder (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-234017) filed on September 30, 2019)
10.2#	2019 Stock Option and Incentive Plan, and form of award agreements thereunder. (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1/A (File No. 333-234017) filed on October 16, 2019)
10.3#	2019 Employee Stock Purchase Plan. (incorporated by reference to Exhibit 10.3 of the Registrant's Registration Statement on Form S-1/A (File No. 333-234017) filed on October 16, 2019)
10.4#	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.4 of the Registrant's Quarterly Report on Form 10-Q filed on December 5, 2019)
10.5#	Form of Indemnification Agreement between the Registrant and each of its directors (incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.6#	Form of Indemnification Agreement between the Registrant and each of its executive officers (incorporated by reference to Exhibit 10.4 of the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.7+	Amended and Restated License Agreement, dated as of July 23, 2019, among the Registrant, the Trustees of the University of Pennsylvania and the Children's Hospital of Philadelphia (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.8+	Sponsored Research Agreement, dated as of April 23, 2018, between the Registrant and the Trustees of the University of Pennsylvania (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.9+	Sponsored Research Agreement, dated as of April 23, 2018, between the Registrant and the Trustees of the University of Pennsylvania (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)

10.10+	Master Translational Research Services Agreement, dated as of October 2018, between the Registrant and the Trustees of the University of Pennsylvania (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.11+	CAROT Master Services Addendum to Master Translational Research Services Agreement, dated as of February 4, 2019, between the Registrant and the Trustees of the University of Pennsylvania (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.12+	CVPF Master Services Addendum to Master Translational Research Services Agreement, dated as of October 22, 2018, between the Registrant and the Trustees of the University of Pennsylvania (incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.13	Lease, dated as of February 11, 2019, between the Registrant and Brandywine Cira, L.P. (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.14#	Employment Agreement between the Registrant and Steven Nichtberger (incorporated by reference to Exhibit 10.16 to the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.15#	Employment Agreement between the Registrant and Anup Marda (incorporated by reference to Exhibit 10.17 to the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.16#	Employment Agreement between the Registrant and Gwendolyn Binder (incorporated by reference to Exhibit 10.18 to the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.17#	Employment Agreement between the Registrant and David Chang (incorporated by reference to Exhibit 10.19 to the Registrant's Registration Statement on Form S-1, filed with the SEC on September 30, 2019)
10.18#*	Amended and Restated Non-Employee Director Compensation Policy
10.19#	Amendment No. 1, dated May 27, 2020, to the Sponsored Research Agreement, dated April 23, 2018, between the Registrant and the Trustees of the University of Pennsylvania (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-39103) filed on May 28, 2020)
10.20+	First Amendment, dated May 27, 2020, to the Amended and Restated License Agreement, dated July 23, 2019, among the Registrant, the Trustees of the University of Pennsylvania and the Children's Hospital of Philadelphia (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-39103) filed on May 28, 2020)
10.21+	Amendment to CAROT Master Services Addendum to Master Translational Research Services Agreement, dated as of May 18, 2020 between the Registrant and the Trustees of the University of Pennsylvania (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39103) filed on August 6, 2020)
10.22+	Amendment No. 2, dated August 17, 2020, to the Sponsored Research Agreement, dated April 23, 2018, as amended by Amendment No. 1 dated May 27, 2020, between the Registrant and the Trustees of the University of Pennsylvania (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39103) filed on November 10, 2020)

10.23+	Amendment No. 1, dated April 27, 2021, to the Sponsored Research Agreement, dated April 23, 2018, between the Registrant and the Trustees of the University of Pennsylvania (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39103) filed on May 3, 2021)
10.24+	Amendment No. 2, dated October 19, 2021, to the Sponsored Research Agreement, dated April 23, 2018, between the Registrant and the Trustees of the University of Pennsylvania (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39103) filed on November 1, 2021)
10.25+	Second Amendment, dated October 19, 2021, to the First Amended and Restated License Agreement, dated May 27, 2020, among the Registrant, the Trustees of the University of Pennsylvania and the Children's Hospital of Philadelphia (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39103) filed on November 1, 2021)
10.26*	First Amendment, dated February 15, 2022, to the Lease, dated as of February 11, 2019, between the Registrant and Brandywine Cira, L.P.
10.27+*	Amendment No. 3, dated December 17, 2021, to the Sponsored Research Agreement, dated April 23, 2018, between the Registrant and the Trustees of the University of Pennsylvania
10.28#*	Form of Employment Agreement
10.29+*	Sponsored Research Agreement, dated as of December 23, 2021, between the Registrant and the Trustees of the University of Pennsylvania
10.30+*	Option Agreement, dated December 23, 2021, by and between Registrant and the Trustees of the University of Pennsylvania
10.31+*	Licence and Supply Agreement, dated December 30, 2021, by and between the Registrant and Oxford Biomedica (UK) Limited
21.1*	List of Subsidiaries of the Registrant
23.1*	Consent of Ernst & Young, independent registered public accounting firm
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended
32.1**	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to 18 U.S.C. Section 1350, as adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2**	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to 18 U.S.C. Section 1350, as adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document

104*	Cover Page Interactive Data File (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101*)

#	Management Contract or compensatory plan or arrangement.
+	Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10) of Regulation S-K.
*	Filed herewith.
**	The certifications furnished in Exhibit 32.1 and 32.2 hereto are deemed to accompany this Annual Report on Form 10-K and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

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 Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Cabaletta Bio, Inc.

Date: March 17, 2022

By: /s/ Steven Nichtberger
Steven Nichtberger, M.D.
Chief Executive Officer and President

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Annual Report on Form 10-K 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/ Steven Nichtberger **Steven Nichtberger, M.D.**	*Director, Chief Executive Officer and President (Principal Executive Officer)*	March 17, 2022
/s/ Anup Marda **Anup Marda**	*Chief Financial Officer (Principal Financial and Accounting Officer)*	March 17, 2022
/s/ Catherine Bollard **Catherine Bollard, M.D.**	*Director*	March 17, 2022
/s/ Scott Brun **Scott Brun, M.D.**	*Director*	March 17, 2022
/s/ Richard Henriques **Richard Henriques**	*Director*	March 17, 2022
/s/ Mark Simon **Mark Simon**	*Director*	March 17, 2022

Exhibit 10.18

CABALETTA BIO, INC.

AMENDED AND RESTATED NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

The purpose of this Amended and Restated Non-Employee Director Compensation Policy of Cabaletta Bio, Inc. (the "Company"), is to provide a total compensation package that enables the Company to attract and retain, on a long-term basis, high-caliber directors who are not employees or officers of the Company or its subsidiaries. In furtherance of the purpose stated above, all non-employee directors shall be paid compensation for services provided to the Company as set forth below:

Cash Retainers

Annual Retainer for Board Membership: $40,000 for general availability and participation in meetings and conference calls of our Board of Directors, to be paid quarterly in arrears, pro- rated based on the number of actual days served by the director during such calendar quarter.

Additional Retainers for Committee Membership:

Audit Committee Chair:	$	15,000
Audit Committee member:	$	7,500
Compensation Committee Chair:	$	10,000
Compensation Committee member:	$	5,000
Nominating and Corporate Governance Committee Chair:	$	8,000
Nominating and Corporate Governance Committee member:	$	4,000

Note: Chair and committee member retainers are in addition to retainers for members of the Board of Directors.

Equity Retainers

Initial Award: An initial, one-time stock option award (the "Initial Award") of 44,000 shares will be granted to each new non-employee director upon his or her election to the Board of Directors, which shall vest in equal quarterly installments over three years from the date of vesting commencement, provided, however, that all vesting shall cease if the director resigns from the Board of Directors or otherwise ceases to serve as a director of the Company. The Initial Award shall expire ten years from the date of grant, and shall have a per share exercise price equal to the Fair Market Value (as defined in the Company's 2019 Stock Option and Incentive Plan) of the Company's common stock on the date of grant. This Initial Award applies only to non-employee directors who are first elected to the Board of Directors subsequent to the Company's initial public offering.

Annual Award: Commencing in 2021, on each date of the Company's Annual Meeting of Stockholders following the completion of the Company's initial public offering (the "Annual Meeting"), each continuing non-employee member of the Board of Directors, other than a director receiving an Initial Award, will receive an annual stock option award (the "Annual Award") of 22,000 shares, which shall vest in full upon the earlier to occur of the first anniversary of the date of grant or the date of the next Annual Meeting; provided, however, that all vesting shall cease if the director resigns from the Board of Directors or otherwise ceases to serve as a director, unless the Board of Directors determines that the circumstances warrant continuation of vesting. Such Annual Award shall expire ten years from the date of grant, and shall have a per share exercise price equal to the Fair Market Value (as defined in the Company's 2019 Stock Option and Incentive Plan) of the Company's common stock on the date of grant.

Each Initial Award and Annual Award will become immediately vested and exercisable upon a Sale Event (as defined in the Company's 2019 Stock Option and Incentive Plan).

Expenses

The Company will reimburse all reasonable out-of-pocket expenses incurred by non- employee directors in attending meetings of the Board or any Committee.

Adopted October 14, 2019, and effective as of October 24, 2019

Amended and restated effective as of December 7, 2021.

FIRST AMENDMENT TO LEASE

THIS FIRST AMENDMENT TO LEASE ("Amendment") is made and entered into as of February 15, 2022, by and between**BRANDYWINE CIRA, L.P.**, a Pennsylvania limited partnership ("Landlord"), and **CABALETTA BIO, INC.**, a Delaware corporation ("Tenant").

A. Landlord and Tenant are parties to a Lease ("Current Lease") dated as of February 11, 2019, for the Premises deemed to contain 7,672 rentable square feet presently known as Suite 600 in the Building known as Cira Centre located at 2929 Arch Street, Philadelphia, Pennsylvania. The Current Lease as amended by this Amendment is referred to herein as the "Lease".

B. The Term currently expires on July 31, 2022. Landlord and Tenant agree to amend the Current Lease to extend the Term upon the terms and conditions set forth herein.

NOW, THEREFORE, in consideration of the mutual covenants and agreements contained herein, and intending to be legally bound, Landlord and Tenant hereby agree as follows:

1. Incorporation of Recitals; Definitions. The recitals set forth above are hereby incorporated herein by reference as if set forth in full in the body of this Amendment. Capitalized terms used but not otherwise defined in this Amendment have the respective meanings given to them in the Current Lease.

2. Term. The Term is hereby extended by an additional 35 months, for the period commencing on August 1, 2022, and terminating on June 30, 2025. Any and all options of Tenant to extend the Term, or expand or reduce the size of the Premises, including without limitation rights of first refusal, offer, and negotiation, are hereby deleted in their entireties and are of no further force and effect.

3. Fixed Rent. Effective on August 1, 2022, "Fixed Rent" shall mean the fixed rent in the amounts set forth below:

Time Period	Annual Fixed Rent Per Rentable Square Foot of Premises	Annualized Fixed Rent	Monthly Fixed Rent
8/1/22 – 12/31/22 ("Fixed Rent Abatement Period")	$0.00	$0.00	$0.00
1/1/23 – 12/31/23	$36.43	$279,490.96	$23,290.91
1/1/24 – 12/31/24	$37.34	$286,472.48	$23,872.71
1/1/25 – 6/30/25	$38.27	$293,607.44	$24,467.29

During the Fixed Rent Abatement Period, Fixed Rent and Tenant's Share of Operating Expenses are abated in full but Tenant shall pay to Landlord: (i) utilities as set forth in the Lease; and (ii) use and occupancy taxes. Notwithstanding the foregoing, if at any time during the Term an Event of Default occurs, then the abatement of Fixed Rent provided above immediately becomes void, and the monthly Fixed Rent during the Fixed Rent Abatement Period equals $23,290.91.

4. Condition of Premises. Tenant acknowledges and agrees that Landlord has no obligation under the Lease to make any improvements to or perform any work in the Premises, or provide any improvement allowance, and Tenant accepts the Premises in their current "AS IS" condition.

5. Relocation. The first sentence of Section 24 of the Current Lease is hereby deleted in its entirety and replaced with the following:

"RELOCATION. Landlord, at its sole expense, on at least 6 months' prior written notice to Tenant,

may require Tenant to move from the Premises to another suite of substantially comparable size and décor in the Building, considering Tenant's use of existing furniture at the time of relocation."

6. Brokers. Landlord and Tenant each represents and warrants to the other that such representing party has had no dealings, negotiations, or consultations with respect to the Premises or this transaction with any broker or finder other than a Landlord affiliate, representing Landlord. Each party must indemnify, defend, and hold harmless the other from and against any and all liability, cost, and expense (including reasonable attorneys' fees and court costs), arising out of or from or related to its misrepresentation or breach of warranty under this Section. This Section will survive the expiration or earlier termination of the Term.

7. Notices. The current address for notices to Landlord under the Lease are set forth below:

Brandywine Cira, L.P.
c/o Brandywine Realty Trust
Attn: Legal Notices/Legal Dept., RE: Building 150
Cira Centre
2929 Arch St., Suite 1800
Philadelphia, PA 19104
Phone: 610-325-5600
Email: Legal.Notices@bdnreit.com

8. Effect of Amendment; Ratification. Landlord and Tenant hereby acknowledge and agree that, except as provided in this Amendment, the Current Lease has not been modified, amended, canceled, terminated, released, superseded, or otherwise rendered of no force or effect. The Current Lease is hereby ratified and confirmed by the parties hereto, and every provision, covenant, condition, obligation, right, term, and power contained in and under the Current Lease continues in full force and effect, affected by this Amendment only to the extent of the amendments and modifications set forth herein. In the event of any conflict between the terms and conditions of this Amendment and those of the Current Lease, the terms and conditions of this Amendment control. To the extent permitted by applicable law, Landlord and Tenant hereby waive trial by jury in any action, proceeding, or counterclaim brought by either against the other on any matter arising out of or in any way connected with the Lease, the relationship of Landlord and Tenant, or Tenant's use or occupancy of the Building, any claim or injury or damage, or any emergency or other statutory remedy with respect thereto. Tenant specifically acknowledges and agrees that the Confession of Judgment provisions of the Current Lease are restated in full below:

In addition to, and not in lieu of any of the foregoing rights granted to Landlord:

(1) WHEN THIS LEASE OR TENANT'S RIGHT OF POSSESSION SHALL BE TERMINATED BY COVENANT OR CONDITION BROKEN, OR FOR ANY OTHER REASON, EITHER DURING THE TERM OF THIS LEASE OR ANY RENEWAL OR EXTENSION THEREOF, AND ALSO WHEN AND AS SOON AS THE TERM HEREBY CREATED OR ANY EXTENSION THEREOF SHALL HAVE EXPIRED, IT SHALL BE LAWFUL FOR ANY ATTORNEY AS ATTORNEY FOR TENANT TO FILE AN AGREEMENT FOR ENTERING IN ANY COMPETENT COURT AN ACTION TO CONFESS JUDGMENT IN EJECTMENT AGAINST TENANT AND ALL PERSONS CLAIMING UNDER TENANT, WHEREUPON, IF LANDLORD SO DESIRES, A WRIT OF EXECUTION OR OF POSSESSION MAY ISSUE FORTHWITH, WITHOUT ANY PRIOR WRIT OF PROCEEDINGS, WHATSOEVER, AND PROVIDED IF FOR ANY REASON AFTER SUCH ACTION SHALL HAVE BEEN COMMENCED THE SAME SHALL BE DETERMINED AND THE POSSESSION OF THE PREMISES HEREBY DEMISED REMAIN IN OR BE RESTORED TO TENANT, LANDLORD SHALL HAVE THE RIGHT UPON ANY SUBSEQUENT DEFAULT OR DEFAULTS, OR UPON THE TERMINATION OF THIS LEASE AS HEREINBEFORE SET FORTH, TO BRING ONE OR MORE ACTION OR ACTIONS AS HEREINBEFORE SET FORTH TO RECOVER POSSESSION OF THE SAID PREMISES.

(2) In any action to confess judgment in ejectment, Landlord shall first cause to be filed in such action an affidavit made by it or someone acting for it setting forth the facts necessary to authorize the entry of judgment, of which facts such affidavit shall be conclusive evidence, and if a true copy of this Lease (and of the truth of the copy such affidavit shall be sufficient evidence) be filed in such action, it shall not be necessary to

file the original as a warrant of attorney, any rule of Court, custom or practice to the contrary notwithstanding.Tenant represents to Landlord that it has a gross income of at least $10,000.

TENANT WAIVER. TENANT SPECIFICALLY ACKNOWLEDGES THAT TENANT HAS VOLUNTARILY, KNOWINGLY, AND INTELLIGENTLY WAIVED CERTAIN DUE PROCESS RIGHTS TO A PREJUDGMENT HEARING BY AGREEING TO THE TERMS OF THE FOREGOING PARAGRAPHS REGARDING CONFESSION OF JUDGMENT. TENANT FURTHER SPECIFICALLY AGREES THAT IN THE EVENT OF DEFAULT, LANDLORD MAY PURSUE MULTIPLE REMEDIES INCLUDING OBTAINING POSSESSION PURSUANT TO A JUDGMENT BY CONFESSION. FURTHERMORE, TENANT SPECIFICALLY WAIVES ANY CLAIM AGAINST LANDLORD AND LANDLORD'S COUNSEL FOR VIOLATION OF TENANT'S CONSTITUTIONAL RIGHTS IN THE EVENT THAT JUDGMENT IS CONFESSED PURSUANT TO THIS LEASE.

TENANT: CABALETTA BIO, INC.

By: **/s/Anup Marda**

Name: **Anup Marda**

Title: **Chief Financial Officer**

Date: **15 February 2022**

9. Representations. Each of Landlord and Tenant represents and warrants to the other that the individual executing this Amendment on such party's behalf is authorized to do so. Tenant and Landlord hereby represent and warrant to each other that, to their respective knowledge, neither party is in default under the Current Lease, nor any event that with the giving of notice or the passage of time, or both, will constitute a default under the Current Lease.

10. Counterparts; Electronic Transmittal. This Amendment may be executed in any number of counterparts, each of which when taken together will be deemed to be one and the same instrument. The parties acknowledge and agree that notwithstanding any law or presumption to the contrary, the exchange of copies of this Amendment and signature pages by electronic transmission will constitute effective execution and delivery of this Amendment for all purposes, and signatures of the parties hereto transmitted and/or produced electronically will be deemed to be their original signature for all purposes.

11. OFAC. Each party hereto represents and warrants to the other that such party is not a party with whom the other is prohibited from doing business pursuant to the regulations of the Office of Foreign Assets Control ("OFAC") of the U.S. Department of the Treasury, including those parties named on OFAC's Specially Designated Nationals and Blocked Persons List. Each party hereto is currently in compliance with, and must at all times during the Term remain in compliance with, the regulations of OFAC and any other governmental requirement relating thereto. Each party hereto must defend, indemnify, and hold harmless the other from and against any and all claims, damages, losses, risks, liabilities and expenses (including reasonable attorneys' fees and costs) incurred by the other to the extent arising from or related to any breach of the foregoing certifications. The foregoing indemnity obligations will survive the expiration or earlier termination of the Lease.

[SIGNATURES ON FOLLOWING PAGE]

IN WITNESS WHEREOF, Landlord and Tenant have duly executed this Amendment as of the date first-above written.

LANDLORD:
BRANDYWINE CIRA, L.P.

By: Brandywine Cira, L.L.C., its general partner

By: /s/Stephen P. Rush
Name: Steven P. Rush
Title: Vice President, Leasing
Date: 16 February 2022

TENANT:
CABALETTA BIO, INC.

By: /s/Anup Marda
Name: Anup Marda
Title: Chief Financial Officer
Date: 15 February 2022

Exhibit 10.27

CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND REPLACED WITH "[***]". SUCH IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS (I) NOT MATERIAL AND (II) THE TYPE OF INFORMATION THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

AMENDMENT NO. 3 TO SPONSORED RESEARCH AGREEMENT

This Amendment No. 3 to the Sponsored Research Agreement (" **Amendment 3**") by and between by and between The Trustees of the University of Pennsylvania, a Pennsylvania nonprofit corporation ("**Penn**"), with offices located at Penn Center for Innovation, 3600 Civic Center Blvd, 9th Floor, Philadelphia, PA 19104-4310, and Cabaletta Bio, Inc., a Delaware corporation **,** having a place of business at 2929 Arch Street, Suite 600, Philadelphia, PA 19104 (formerly Tycho Therapeutics, Inc., a Delaware corporation having a place of business at 501 Northwick Lane, Villanova, PA 19085) ("**Sponsor**") is effective as of December 17, 2021 (" **Amendment Effective Date**"). Penn and Sponsor may be referred to herein as a " **Party**" or, collectively, as "**Parties**."

Penn and Sponsor may be referred to herein as a " **Party**" or, collectively, as "**Parties**".

RECITALS:

WHEREAS, the Parties entered into a Sponsored Research Agreement dated April 23, 2018 (" **Agreement**"), as amended by Amendment No. 1 dated May 1, 2020 ("**Amendment 1**") and Amendment No. 2 dated May 1, 2020 (" **Amendment 2**"). Capitalized terms used but not defined herein shall have the meanings ascribed to them in the Agreement, as amended by Amendment 1 and Amendment 2; and

WHEREAS, the Parties now desire to amend the Agreement as set forth herein.

NOW, THEREFORE, in consideration of the various promises and undertakings set forth herein, the Parties agree as follows:

1. **Scope of work**.

   The scope of work to be performed in accordance with the Agreement, as amended by Amendment 1 and Amendment 2, is hereby supplemented to add to the additional workplan detailed in Attachment A-2 hereto ("**Amendment 3 Workplan**").

2. **Term.** Section 7.1 of the Agreement is hereby deleted and replaced with the following:

   "**Term.** (a) The term of this Agreement as it applies to the Original Workplan shall begin on the Effective Date of the Agreement (April 23, 2018) and shall end on [***] unless terminated sooner pursuant to Sections 2.2 or 7.2 of the Agreement.

   (b) The term of this Agreement as it applies to the Supplemental Workplan shall begin on the [***] and shall end on [***] unless terminated sooner pursuant to Sections 2.2 or 7.2 of the Agreement.

(c) The term of this Agreement as it applies to the Amendment 3 Workplan shall begin on the [***] and shall end [***] unless terminated sooner pursuant to Sections 2.2 or 7.2 of the Agreement.

(d) The term of the Agreement as it applies to the Original Workplan, the Supplemental Workplan, or the Amendment 3 Workplan may be extended or renewed only by mutual written agreement signed by duly authorized representatives of both Parties."

3. **Budget and Payment Terms.** The total budget for the Amendment 3 Workplan is detailed in Exhibit 2 to Attachment A-2.

4. **Entire Agreement of the Parties; Amendments** . The Agreement, including any Exhibits and as amended by Amendment 1, Amendment 2 and Amendment 3, constitutes and contains the entire understanding and agreement of the Parties respecting the subject matter hereof and cancel and supersedes any and all prior negotiations, correspondence, understandings and agreements between the Parties, whether oral or written, regarding such subject matter. No waiver, modification or amendment of any provision of the Agreement and/or Amendment 1, Amendment 2, and/or this Amendment 3 shall be valid or effective unless made in a writing referencing the Agreement and/or this Amendment 1, this Amendment 2, and/or this Amendment 3 and signed by a duly authorized officer of each Party.

5. **Counterparts** . This Amendment 3 may be executed in counterparts, each of which will be deemed an original, and all of which together will be deemed to be one and the same instrument. A portable document format (PDF) or electronic copy of this Amendment 3, including the signature pages, will be deemed an original.

IN WITNESS WHEREOF, the duly authorized representatives of the Parties hereby execute this Amendment as of the date first written above.

THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA

By: [***]Name: [***]Title: [***]

CABALETTA BIO, INC.

By: /s/ Steven Nichtberger
Name: Steven Nichtberger, M.D.
Title: President and CEO

I have read and understood the responsibilities of the Principal Investigator:

By: /s/ Aimee Payne
Name: Aimee Payne

Attachment A-2

Summary of Supplemental Sponsored Research

Scope of Work:

Detailed in Exhibit 1 hereto

Principal Investigator – [***]

Representative of Sponsor – [***]

Report Schedule:

For final report of Phase 1 within [***]after completion of Phase 1.

Budget:

Detailed in Exhibit 2 hereto. Payments under this Agreement will be payable within [***] of Sponsor's receipt of an invoice from Penn.

Payment Schedule:

Date Payment Due	Amount of Payment Due
Phase I	
Within [***] of Sponsor's receipt of an invoice to be issued on the [***]	$[***]

Exhibit 1 to Attachment A-2

[***]

Exhibit 2 to Attachment A-2
Budget

[***]

EMPLOYMENT AGREEMENT

This Employment Agreement ("Agreement") is made between Cabaletta Bio, Inc., a Delaware corporation (the "Company"), and _____ (the "Executive") and is effective [as of the date hereof] [as of the closing of the Company's first underwritten public offering of its equity securities pursuant to an effective registration statement under the Securities Act of 1933, as amended] (the "Effective Date"). [Except with respect to the Restrictive Covenant Agreement and the Equity Documents (each as defined below), this Agreement supersedes in all respects all prior agreements between the Executive and the Company regarding the subject matter herein, including without limitation (i) the letter agreement between the Executive and the Company dated _____ (the "Prior Agreement"), and (ii) any offer letter, employment agreement or severance agreement].

WHEREAS, the Company desires to [continue to] employ the Executive and the Executive desires to [continue to] be employed by the Company on the [new] terms and conditions contained herein.

NOW, THEREFORE, in consideration of the mutual covenants and agreements herein contained and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties agree as follows:

1. Employment.

(a) Term. The Company shall employ the Executive and the Executive shall be employed by the Company pursuant to this Agreement commencing as of the Effective Date and continuing until such employment is terminated in accordance with the provisions hereof (the "Term"). The Executive's employment with the Company will [continue to] be "at will," meaning that the Executive's employment may be terminated by the Company or the Executive at any time and for any reason subject to the terms of this Agreement.

(b) Position and Duties. The Executive shall serve as the [Title] of the Company and shall have such powers and duties as may from time to time be prescribed by the [Board of Directors (the "Board")][1]/[Chief Executive Officer (the "CEO") or other duly authorized executive][2]. [In addition, the Company shall cause the Executive to be nominated for election to the Board and to be recommended to the stockholders for election to the Board as long as the executive remains the Chief Executive Officer of the Company (the "CEO"), provided the Executive shall resign from the Board and from any related positions upon ceasing to serve as CEO for any reason.][3] The Executive shall devote the Executive's full working time and efforts to the business and affairs of the Company. Notwithstanding the foregoing, the Executive may serve on other boards of directors, with the approval of the Board[of Directors of the Company (the "Board")][4], or engage in religious, charitable or other community activities as long as such services and activities are disclosed to the Board and do not interfere with the Executive's performance of the Executive's duties to the Company. To the extent applicable, the Executive shall be deemed to have resigned from all officer and board member positions that the Executive holds with the Company or any of its respective subsidiaries and affiliates upon the termination of the Executive's employment for any reason. The Executive shall execute any documents in reasonable form as may be requested to confirm or effectuate any such resignations.

---

[1] For CEO agreement.
[2] For other executives' agreements.
[3] For CEO agreement.
[4] For other executives' agreements.

2. Compensation and Related Matters.

(a) Base Salary. The Executive's initial base salary shall be paid at the rate of $[_____] per year. [The Executive's base salary will increase to $_____ effective [_____], 20[__], subject to the Executive's continued employment.] The Executive's base salary shall be subject to periodic review by the Board or the Compensation Committee of the Board (the "Compensation Committee"). The base salary in effect at any given time is referred to herein as "Base Salary." The Base Salary shall be payable in a manner that is consistent with the Company's usual payroll practices for executive officers.

(b) Incentive Compensation. The Executive shall be eligible to receive cash incentive compensation as determined by the Board or the Compensation Committee from time to time. The Executive's initial target annual incentive compensation shall be [___] percent of the Executive's Base Salary; [provided that any annual incentive compensation awarded to the Executive with respect to performance in calendar year 2019 will be pro-rated based on (i) the target bonus in effect prior to the Effective Date for the period of time the Executive was employed in calendar year 2019 prior to the Effective Date and (ii) the target bonus set forth in this Section 2(b) for the period of time the Executive is employed between the Effective Date and December 31, 2019.] [The Executive's annual incentive compensation with respect to performance in calendar year [___] will be prorated based on the Effective Date.] The target bonus in effect at any given time is referred to herein as "Target Bonus." The actual amount of the Executive's annual incentive compensation, if any, shall be determined in the sole discretion of the Board or the Compensation Committee, subject to the terms of any applicable incentive compensation plan that may be in effect from time to time. Except as otherwise provided herein, to earn incentive compensation, the Executive must be employed by the Company on the day such incentive compensation is paid.

(c) Expenses. The Executive shall be entitled to receive prompt reimbursement for all reasonable expenses incurred by the Executive during the Term in performing services hereunder, in accordance with the policies and procedures then in effect and established by the Company for its executive officers.

(d) Other Benefits. The Executive shall be eligible to participate in or receive benefits under the Company's employee benefit plans in effect from time to time, subject to the terms of such plans.

(e) Paid Time Off. The Executive shall be eligible to accrue up to [___] weeks of paid vacation per calendar year in accordance with the Company's vacation policy, as in effect from time to time. The Executive shall also be eligible for Company designated holidays.

(f) Equity. [The equity awards held by the Executive shall continue to be governed by the terms and conditions of the Company's applicable equity incentive plan(s) and the applicable award agreement(s) governing the terms of such equity awards held by the Executive (collectively, the "Equity Documents"); provided, however, and] [Subject to the approval of the Board, on or after the Effective Date, the Executive will be granted an incentive stock option to purchase [___] shares of the Company's common stock with an exercise price per share equal to the fair market value of the Company's common stock as determined by the Board on the date of the grant, and subject to vesting and other terms and conditions set forth in the Company's stock option and grant plan (the "Plan") and the applicable stock option agreement (the "Initial Stock Award", and together with the Plan, the "Equity Documents"). The Initial Stock Award shares shall vest as follows: [___], provided that as of each such vesting date the Executive is still providing services to the Company.] [N]otwithstanding anything to the contrary in the Equity Documents, Section 6(a)(ii) of this Agreement shall apply in the event of a termination by the Company without Cause or by the Executive for Good Reason in either event within the Change in Control Period (as such terms are defined below).

3. Termination. The Executive's employment hereunder may be terminated without any breach of this Agreement under the following circumstances:

(a) Death. The Executive's employment hereunder shall terminate upon death.

(b) Disability. The Company may terminate the Executive's employment if the Executive is disabled and unable to perform the essential functions of the Executive's then existing position or positions under this Agreement with or without reasonable accommodation for a period of 180 days (which need not be consecutive) in any 12-month period. If any question shall arise as to whether during any period the Executive is disabled so as to be unable to perform the essential functions of the Executive's then existing position or positions with or without reasonable accommodation, the Executive may, and at the request of the Company shall, submit to the Company a certification in reasonable detail by a physician selected by the Company to whom the Executive or the Executive's guardian has no reasonable objection as to whether the Executive is so disabled or how long such disability is expected to continue, and such certification shall for the purposes of this Agreement be conclusive of the issue. The Executive shall cooperate with any reasonable request of the physician in connection with such certification. If such question shall arise and the Executive shall fail to submit such certification, the Company's determination of such issue shall be binding on the Executive. Nothing in this Section 3(b) shall be construed to waive the Executive's rights, if any, under existing law including, without limitation, the Family and Medical Leave Act of 1993, 29 U.S.C. §2601 *et seq*. and the Americans with Disabilities Act, 42 U.S.C. §12101 *et seq.*

(c) Termination by Company for Cause. The Company may terminate the Executive's employment hereunder for Cause. For purposes of this Agreement, "Cause" shall mean any of the following:

(i) conduct by the Executive in connection with the Executive's service to the Company that is fraudulent or which is grossly negligent;

(ii) the commission by the Executive of acts satisfying the elements of (A) any felony or (B) a misdemeanor involving deceit, dishonesty or fraud related to the Executive's employment;

(iii) the Executive's willful failure or refusal to comply with lawful directives of the [Board]/[CEO or the Board] which, if curable, is not cured by the Executive within 30 days following the Executive's receipt of written notice from the Company;

(iv) the Executive's willful material breach of a written Company policy or the Executive's representations, warranties, covenants and/or obligations under this Agreement or the Restrictive Covenant Agreement;

(v) materially unsatisfactory performance by the Executive which, if curable, is not cured by the Executive within 30 days following the Executive's receipt of written notice from the Company;

(vi) material misconduct by the Executive which discredits or damages the Company or any of its affiliates; and/or

(vii) the Executive's failure to cooperate with a bona fide internal investigation or an investigation by regulatory or law enforcement authorities, after being instructed by the Company to cooperate, or the willful destruction or failure to preserve documents or other materials known to be relevant to such investigation or the inducement of others to fail to cooperate or to produce documents or other materials in connection with such investigation.

(d) Termination by the Company without Cause. The Company may terminate the Executive's employment hereunder at any time without Cause. Any termination by the Company of the Executive's employment under this Agreement which does not constitute a termination for Cause under Section 3(c) and does not result from the death or disability of the Executive under Section 3(a) or (b) shall be deemed a termination without Cause.

(e) Termination by the Executive. The Executive may terminate employment hereunder at any time for any reason, including but not limited to, Good Reason. For purposes of this Agreement, "Good Reason" shall mean that the Executive has completed all steps of the Good Reason Process (hereinafter defined) following the first occurrence of any of the following events without the Executive's consent (each, a "Good Reason Condition"):

(i) a material diminution in the Executive's responsibilities, authority or duties [, in each case within the 12 months following a Change in Control];[5]

(ii) a material diminution in the Executive's Base Salary;

(iii) a relocation of the Executive's principal place of employment by more than 50 miles from the current location; or

(iv) a material breach of this Agreement by the Company.

The "Good Reason Process" consists of the following steps:

(i) the Executive reasonably determines in good faith that a Good Reason Condition has occurred;

(ii) the Executive notifies the Company in writing of the first occurrence of the Good Reason Condition within 90 days of such condition;

(iii) the Executive cooperates in good faith with the Company's efforts, for a period of not less than 30 days following such notice (the "Cure Period"), to remedy the Good Reason Condition;

(iv) notwithstanding such efforts, the Good Reason Condition continues to exist; and

(v) the Executive terminates employment within 30 days after the end of the Cure Period.

If the Company cures the Good Reason Condition during the Cure Period, Good Reason shall be deemed not to have occurred.

If the Executive's employment with the Company is terminated for any reason, the Company shall pay or provide to the Executive (or to the Executive's authorized representative or estate) (i) any Base Salary plus any accrued but unused vacation, earned through the Date of Termination; (ii) unpaid expense reimbursements (subject to, and in accordance with, Section 2(c) of this Agreement); and (iii) any vested benefits the Executive may have under any employee benefit plan of the Company through the Date of Termination, which vested benefits shall be paid and/or provided in accordance with the terms of such employee benefit plans (collectively, the "Accrued Obligations").

4. Notice and Date of Termination.

(a) Notice of Termination

[5] Bracketed language applies only to non-CEO executives.

. Except for termination as specified in Section 3(a), any termination of the Executive's employment by the Company or any such termination by the Executive shall be communicated by written Notice of Termination to the other party hereto. For purposes of this Agreement, a "Notice of Termination" shall mean a notice which shall indicate the specific termination provision in this Agreement relied upon.

(b) Date of Termination. "Date of Termination" shall mean: (i) if the Executive's employment is terminated by death, the date of death; (ii) if the Executive's employment is terminated on account of disability under Section 3(b) or by the Company for Cause under Section 3(c), the date on which Notice of Termination is given; (iii) if the Executive's employment is terminated by the Company without Cause under Section 3(d), the date on which a Notice of Termination is given or the date otherwise specified by the Company in the Notice of Termination; (iv) if the Executive's employment is terminated by the Executive under Section 3(e) other than for Good Reason, 30 days after the date on which a Notice of Termination is given, and (v) if the Executive's employment is terminated by the Executive under Section 3(e) for Good Reason, the date on which a Notice of Termination is given after the end of the Cure Period. Notwithstanding the foregoing, in the event that the Executive gives a Notice of Termination to the Company, the Company may unilaterally accelerate the Date of Termination and such acceleration shall not result in a termination by the Company for purposes of this Agreement.

5. Severance Pay and Benefits Upon Termination by the Company without Cause or by the Executive for Good Reason Outside the Change in Control Period. If the Executive's employment is terminated by the Company without Cause as provided in Section 3(d), or the Executive terminates employment for Good Reason as provided in Section 3(e), each outside of the Change in Control Period (as defined below), then, in addition to the Accrued Obligations, and subject to (i) the Executive signing a separation agreement and release in a form and manner satisfactory to the Company, which shall include, without limitation, a general release of claims against the Company and all related persons and entities, a reaffirmation of all of the Executive's Continuing Obligations (as defined below), and shall provide that if the Executive breaches any of the Continuing Obligations, all payments of the Severance Amount shall immediately cease (the "Separation Agreement and Release"), and (ii) the Separation Agreement and Release becoming irrevocable, all within 60 days after the Date of Termination (or such shorter period as set forth in the Separation Agreement and Release), which shall include a seven (7) day revocation period:

(a) the Company shall pay the Executive an amount equal to [___] months of the Executive's Base Salary (the "Severance Amount"); and

(b) subject to the Executive's copayment of premium amounts at the applicable active employees' rate and the Executive's proper election to receive benefits under the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended ("COBRA"), the Company shall pay to the group health plan provider, the COBRA provider or the Executive a monthly payment equal to the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company until the earliest of (A) the [__] month anniversary of the Date of Termination; (B) the Executive's eligibility for group medical plan benefits under any other employer's group medical plan; or (C) the cessation of the Executive's continuation rights under COBRA; provided, however, if the Company determines that it cannot pay such amounts to the group health plan provider or the COBRA provider (if applicable) without potentially violating

applicable law (including, without limitation, Section 2716 of the Public Health Service Act), then the Company shall convert such payments to payroll payments directly to the Executive for the time period specified above. Such payments shall be subject to tax-related deductions and withholdings and paid on the Company's regular payroll dates.

The amounts payable under Section 5, to the extent taxable, shall be paid out in substantially equal installments in accordance with the Company's payroll practice over [__]6 months commencing within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the Severance Amount, to the extent it qualifies as "non-qualified deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code"), shall begin to be paid in the second calendar year by the last day of such 60-day period; provided, further, that the initial payment shall include a catch-up payment to cover amounts retroactive to the day immediately following the Date of Termination. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2).

6. Severance Pay and Benefits Upon Termination by the Company without Cause or by the Executive for Good Reason within the Change in Control Period. The provisions of this Section 6 shall apply in lieu of, and expressly supersede, the provisions of Section 5 if (i) the Executive's employment is terminated either (a) by the Company without Cause as provided in Section 3(d), or (b) by the Executive for Good Reason as provided in Section 3(e), and (ii) the Date of Termination is within the 60 days before or 12 months after the occurrence of the first event constituting a Change in Control (such period, the "Change in Control Period"). These provisions shall terminate and be of no further force or effect after a Change in Control Period.

(a) If the Executive's employment is terminated by the Company without Cause as provided in Section 3(d) or the Executive terminates employment for Good Reason as provided in Section 3(e) and in each case the Date of Termination occurs during the Change in Control Period, then, in addition to the Accrued Obligations, and subject to the signing of the Separation Agreement and Release by the Executive and the Separation Agreement and Release becoming fully effective, all within the time frame set forth in the Separation Agreement and Release but in no event more than 60 days after the Date of Termination:

(i) the Company shall pay the Executive a lump sum in cash in an amount equal to [___] times the sum of (A) the Executive's then current Base Salary (or the Executive's Base Salary in effect immediately prior to the Change in Control, if higher) plus (B) the Executive's Target Bonus for the then-current year; and

(ii) notwithstanding anything to the contrary in any applicable option agreement or other stock-based award agreement, all time-based stock options and other stock-based awards subject to time-based vesting held by the Executive (the "Time-Based Equity Awards") shall immediately accelerate and become fully exercisable or nonforfeitable as of the later of (i) the Date of Termination or (ii) the effective date of the Separation Agreement and Release (the "Accelerated Vesting Date"); *provided* that any termination or forfeiture of the unvested portion of such Time-Based Equity Awards that

6 This period will match the length of base salary continuation pursuant to (a) above.

would otherwise occur on the Date of Termination in the absence of this Agreement will be delayed until the effective date of the Separation Agreement and Release and will only occur if the vesting pursuant to this subsection does not occur due to the absence of the Separation Agreement and Release becoming fully effective within the time period set forth therein. Notwithstanding the foregoing, no additional vesting of the Time-Based Equity Awards shall occur during the period between the Executive's Date of Termination and the Accelerated Vesting Date; and

(iii) subject to the Executive's copayment of premium amounts at the applicable active employees' rate and the Executive's proper election to receive benefits under COBRA, the Company shall pay to the group health plan provider, the COBRA provider or the Executive a monthly payment equal to the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company until the earliest of (A) the [__] month anniversary of the Date of Termination; (B) the Executive's eligibility for group medical plan benefits under any other employer's group medical plan; or (C) the cessation of the Executive's continuation rights under COBRA; provided, however, if the Company determines that it cannot pay such amounts to the group health plan provider or the COBRA provider (if applicable) without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), then the Company shall convert such payments to payroll payments directly to the Executive for the time period specified above. Such payments shall be subject to tax-related deductions and withholdings and paid on the Company's regular payroll dates.

The amounts payable under this Section 6(a), to the extent taxable, shall be paid or commence to be paid within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, such payments to the extent they qualify as "non-qualified deferred compensation" within the meaning of Section 409A of the Code, shall be paid or commence to be paid in the second calendar year by the last day of such 60-day period. For the avoidance of doubt, in the event that the Executive's Date of Termination is within the 60 days before a Change in Control and the Executive has signed the Separation Agreement and Release that has become irrevocable and is entitled to the benefits under Section 5 of this Agreement, then the Executive will receive the benefits set forth in this Section 6 following the occurrence of a Change in Control; provided that the lump sum amount to be paid to the Executive pursuant to Section 6(a)(i) will be decreased by any benefits previously paid to the Executive pursuant to Section 5, and the Executive will receive no further benefits pursuant to Section 5. In no event may there be duplication of benefits under Section 5 and Section 6.

(b) Additional Limitation.

(i) Anything in this Agreement to the contrary notwithstanding, in the event that the amount of any compensation, payment or distribution by the Company to or for the benefit of the Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a manner consistent with Section 280G of the Code, and the applicable regulations thereunder (the "Aggregate Payments"), would be subject to the excise tax imposed by Section 4999 of

the Code, then the Aggregate Payments shall be reduced (but not below zero) so that the sum of all of the Aggregate Payments shall be $1.00 less than the amount at which the Executive becomes subject to the excise tax imposed by Section 4999 of the Code; provided that such reduction shall only occur if it would result in the Executive receiving a higher After Tax Amount (as defined below) than the Executive would receive if the Aggregate Payments were not subject to such reduction. In such event, the Aggregate Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Aggregate Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 280G of the Code: (1) cash payments not subject to Section 409A of the Code; (2) cash payments subject to Section 409A of the Code; (3) equity-based payments and acceleration; and (4) non-cash forms of benefits; provided that in the case of all the foregoing Aggregate Payments all amounts or payments that are not subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c).

(ii) For purposes of this Section 6(b), the "After Tax Amount" means the amount of the Aggregate Payments less all federal, state, and local income, excise and employment taxes imposed on the Executive as a result of the Executive's receipt of the Aggregate Payments. For purposes of determining the After Tax Amount, the Executive shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes.

(iii) The determination as to whether a reduction in the Aggregate Payments shall be made pursuant to Section 6(b)(i) shall be made by a nationally recognized accounting firm selected by the Company (the "Accounting Firm"), which shall provide detailed supporting calculations both to the Company and the Executive within 15 business days of the Date of Termination, if applicable, or at such earlier time as is reasonably requested by the Company or the Executive. Any determination by the Accounting Firm shall be binding upon the Company and the Executive.

(c) Definitions. For purposes of this Section 6, a "Change in Control" shall mean a "Sale Event" as defined in the Cabaletta Bio, Inc. 2019 Stock Option and Incentive Plan, as may be amended from time to time, but only to the extent such Sale Event is also a "change in control event" within the meaning of Section 409A of the Code and the regulations promulgated thereunder.

7. Section 409A.

(a) Anything in this Agreement to the contrary notwithstanding, if at the time of the Executive's separation from service within the meaning of Section 409A of the Code, the Company determines that the Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that the Executive becomes entitled to under this Agreement or otherwise on account of the Executive's separation

from service would be considered deferred compensation otherwise subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after the Executive's separation from service, or (B) the Executive's death. If any such delayed cash payment is otherwise payable on an installment basis, the first payment shall include a catch-up payment covering amounts that would otherwise have been paid during the six-month period but for the application of this provision, and the balance of the installments shall be payable in accordance with their original schedule.

(b) All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by the Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year (except for any lifetime or other aggregate limitation applicable to medical expenses). Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(c) To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon the Executive's termination of employment, then such payments or benefits shall be payable only upon the Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

(d) The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. Each payment pursuant to this Agreement or the Restrictive Covenant Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2). The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

(e) The Company makes no representation or warranty and shall have no liability to the Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

8. Continuing Obligations.

(a) Restrictive Covenant Agreement. [The terms of] [As a condition of employment, the Executive is required to enter into] the Employee Restrictive Covenant Agreement, [dated [_____]] (the "Restrictive Covenant Agreement"), between the Company and the Executive, attached hereto as Exhibit A, [continue to be in full force and effect and are] [which are] incorporated by reference as material terms of this Agreement. For purposes of this Agreement, the obligations in this Section 8 and those that arise in the Restrictive Covenant Agreement and any other agreement relating to confidentiality, assignment of inventions, or other restrictive covenants shall collectively be referred to as the "Continuing Obligations."

(b) Third-Party Agreements and Rights. The Executive hereby confirms that the Executive is not bound by the terms of any agreement with any previous employer or other party which restricts in any way the Executive's use or disclosure of information, other than confidentiality restrictions (if any), or the Executive's engagement in any business. The Executive represents to the Company that the Executive's execution of this Agreement, the Executive's employment with the Company and the performance of the Executive's proposed duties for the Company will not violate any obligations the Executive may have to any such previous employer or other party. In the Executive's work for the Company, the Executive will not disclose or make use of any information in violation of any agreements with or rights of any such previous employer or other party, and the Executive will not bring to the premises of the Company any copies or other tangible embodiments of non-public information belonging to or obtained from any such previous employment or other party.

(c) Litigation and Regulatory Cooperation. During and after the Executive's employment, the Executive shall cooperate fully with the Company in (i) the defense or prosecution of any claims or actions now in existence or which may be brought in the future against or on behalf of the Company which relate to events or occurrences that transpired while the Executive was employed by the Company, and (ii) the investigation, whether internal or external, of any matters about which the Company believes the Executive may have knowledge or information. The Executive's full cooperation in connection with such claims, actions or investigations shall include, but not be limited to, being available to meet with counsel to answer questions or to prepare for discovery or trial and to act as a witness on behalf of the Company at mutually convenient times. During and after the Executive's employment, the Executive also shall cooperate fully with the Company in connection with any investigation or review of any federal, state or local regulatory authority as any such investigation or review relates to events or occurrences that transpired while the Executive was employed by the Company. The Company shall reimburse the Executive for any reasonable out-of-pocket expenses incurred in connection with the Executive's performance of obligations pursuant to this Section 8(c).

(d) Relief. The Executive agrees that it would be difficult to measure any damages caused to the Company which might result from any breach by the Executive of the Continuing Obligations, and that in any event money damages would be an inadequate remedy for any such breach. Accordingly**,** the Executive agrees that if the Executive breaches, or proposes to breach, any portion of the Continuing Obligations, the Company shall be entitled, in addition to all other remedies that it may have, to an injunction or other appropriate equitable

relief to restrain any such breach without showing or proving any actual damage to the Company.

(e) Protected Disclosures and Other Protected Action. Nothing in this Agreement shall be interpreted or applied to prohibit the Executive from making any good faith report to any governmental agency or other governmental entity (a "Government Agency") concerning any act or omission that the Executive reasonably believes constitutes a possible violation of federal or state law or making other disclosures that are protected under the anti-retaliation or whistleblower provisions of applicable federal or state law or regulation. In addition, nothing contained in this Agreement limits the Executive's ability to communicate with any Government Agency or otherwise participate in any investigation or proceeding that may be conducted by any Government Agency, including the Executive's ability to provide documents or other information, without notice to the Company. In addition, for the avoidance of doubt, pursuant to the federal Defend Trade Secrets Act of 2016, the Executive shall not be held criminally or civilly liable under any federal or state trade secret law or under this Agreement or the Restrictive Covenant Agreement for the disclosure of a trade secret that (a) is made (i) in confidence to a federal, state, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (b) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal.

9. Consent to Jurisdiction. The parties hereby consent to the jurisdiction of the state and federal courts of the Commonwealth of Pennsylvania. Accordingly, with respect to any such court action, the Executive (a) submits to the personal jurisdiction of such courts; (b) consents to service of process; and (c) waives any other requirement (whether imposed by statute, rule of court, or otherwise) with respect to personal jurisdiction or service of process.

10. Integration. This Agreement constitutes the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior agreements between the parties concerning such subject matter[, including the Prior Agreement, provided that the Restrictive Covenant Agreement, and the Equity Documents remain in full force and effect].

11. Withholding; Tax Effect. All payments made by the Company to the Executive under this Agreement shall be net of any tax or other amounts required to be withheld by the Company under applicable law. Nothing in this Agreement shall be construed to require the Company to make any payments to compensate the Executive for any adverse tax effect associated with any payments or benefits or for any deduction or withholding from any payment or benefit.

12. Assignment. Neither the Executive nor the Company may make any assignment of this Agreement or any interest in it, by operation of law or otherwise, without the prior written consent of the other; provided, however, that the Company may assign its rights and obligations under this Agreement (including the Restrictive Covenant Agreement) without the Executive's consent to any affiliate or to any person or entity with whom the Company shall hereafter effect a reorganization, consolidate with, or merge into or to whom it transfers all or substantially all of its properties or assets; provided further that if the Executive remains employed or becomes employed by the Company, the purchaser or any of their affiliates in connection with any such

transaction, then the Executive shall not be entitled to any payments, benefits or vesting pursuant to Section 5 or pursuant to Section 6 of this Agreement. This Agreement shall inure to the benefit of and be binding upon the Executive and the Company, and each of the Executive's and the Company's respective successors, executors, administrators, heirs and permitted assigns.

13. Enforceability. If any portion or provision of this Agreement (including, without limitation, any portion or provision of any section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

14. Survival. The provisions of this Agreement shall survive the termination of this Agreement and/or the termination of the Executive's employment to the extent necessary to effectuate the terms contained herein.

15. Waiver. No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement, or the waiver by any party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

16. Notices. Any notices, requests, demands and other communications provided for by this Agreement shall be sufficient if in writing and delivered in person or sent by a nationally recognized overnight courier service or by registered or certified mail, postage prepaid, return receipt requested, to the Executive at the last address the Executive has filed in writing with the Company or, in the case of the Company, at its main offices, attention of the Board.

17. Amendment. This Agreement may be amended or modified only by a written instrument signed by the Executive and by a duly authorized representative of the Company.

18. Effect on Other Plans and Agreements. An election by the Executive to resign for Good Reason under the provisions of this Agreement shall not be deemed a voluntary termination of employment by the Executive for the purpose of interpreting the provisions of any of the Company's benefit plans, programs or policies. Nothing in this Agreement shall be construed to limit the rights of the Executive under the Company's benefit plans, programs or policies except as otherwise provided in Section 8 hereof, and except that the Executive shall have no rights to any severance benefits under any Company severance pay plan, offer letter or otherwise. In the event that the Executive is party to an agreement with the Company providing for payments or benefits under such plan or agreement and under this Agreement, the terms of this Agreement shall govern and the Executive may receive payment under this Agreement only and not both. Further, Section 5 and Section 6 of this Agreement are mutually exclusive and in no event shall the Executive be entitled to payments or benefits pursuant to both Section 5 and Section 6 of this Agreement.

19. Governing Law. This is a Pennsylvania contract and shall be construed under and be governed in all respects by the laws of the Commonwealth of Pennsylvania without giving effect to the conflict of laws principles thereof. With respect to any disputes concerning federal law, such disputes shall be determined in accordance with the law as it would be interpreted and applied by the United States Court of Appeals for the Third Circuit.

20. [Conditions. Notwithstanding anything to the contrary herein, the effectiveness of this Agreement shall be conditioned on (i) the Executive's satisfactory completion of reference and background checks, if so requested by the Company, and (ii) the Executive's submission of satisfactory proof of the Executive's legal authorization to work in the United States.]

21. Counterparts. This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original; but such counterparts shall together constitute one and the same document.

IN WITNESS WHEREOF, the parties have executed this Agreement effective on the Effective Date.

CABALETTA BIO, INC.

By: _____

Its: _____

[EXECUTIVE]

_____

[Name]

Exhibit A

Employee Restrictive Covenant Agreement

ACTIVE/100854405.3

CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND REPLACED WITH "[***]". SUCH IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS (I) NOT MATERIAL AND (II) THE TYPE OF INFORMATION THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

SPONSORED RESEARCH AGREEMENT

This Sponsored Research Agreement ("**Agreement**") is dated as of December 23, 2021 (the "**Effective Date**") by and between The Trustees of the University of Pennsylvania, a Pennsylvania nonprofit corporation ("**Penn**"), with offices located at Penn Center for Innovation, 3600 Civic Center Blvd, 9th Floor, Philadelphia, PA 19104-4310, and Cabaletta Bio, Inc., a Delaware corporation (" **Sponsor**"), having a place of business at 2929 Arch Street, Suite 600, Philadelphia, PA 19104. Penn and Sponsor may be referred to herein as a "**Party**" or, collectively, as "**Parties**".

RECITALS:

WHEREAS, Penn and Sponsor are entering into this Agreement since Sponsor desires to fund the research of Drew Weissman, MD, PhD of Penn's Perelman School of Medicine in certain specific areas;

WHEREAS, Sponsor desires to support such research conducted by Penn in accordance with the terms and conditions of this Agreement;

WHEREAS, the research program contemplated by this Agreement is of mutual interest to Sponsor and Penn and furthers the educational, scholarship and research objectives of Penn as a nonprofit, tax-exempt, educational institution, and may benefit both Sponsor and Penn through the creation or discovery of new inventions;

WHEREAS, the Parties, have entered into a license agreement and sponsored research agreements for the development and commercialization of chimeric autoantibody receptor (CAAR) T cells; and

WHEREAS, the Parties have entered into an option agreement concurrently with this Agreement for certain patent rights related to targeted mRNA-LNP technology invented by Drew Weissman MD, PhD and others at Penn.

NOW, THEREFORE, in consideration of the various promises and undertakings set forth herein, the Parties agree as follows:

ARTICLE 1
DEFINITIONS

1.1 "**Antigen Group I**" means [***].

1.2 "**Antigen Group II**" means [***].

1.3 "**Background IP Option Agreement**" means the option agreement between the Parties with the same Effective Date as the Agreement related to targeted mRNA-LNP technology invented in the Weissman laboratory at Penn.

1.4 "**mRNA Chimeric Autoantibody Receptor Product**" or "**mRNA CAAR Product**" means [***].

1.5 "**Chimeric Autoantibody Receptor T Cell Product**" or "**CAAR T Product**" means [***].

1.6 "**mRNA Chimeric Autoantibody Receptor T Cell Product**" or "**mRNA CAAR T Product**" is a [***].

1.7 "**CAAR-Potentiating mRNA Vaccine Product**" means [***].

1.8 "**Field of Use**" means the following subfields (each a "Subfield"): [***].

1.9 "**License Agreement**" means the Cabaletta Amended and Restated License Agreement (**CARLA**) effective July 23, 2019 by and among Penn, CHOP, and Cabaletta Bio, as amended by its First Amendment dated May 1, 2020 and its Second Amendment dated October 19, 2021.

1.10 "**mRNA-Enabled CAAR Products**" means [***].

1.11 "**Penn Intellectual Property**" means Related Intellectual Property and Unrelated Intellectual Property, each as defined below.

1.12 "**Principal Investigator**" means Drew Weissman, MD, PhD who has agreed to serve as faculty investigator for the Sponsored Research and shall be responsible for the conduct, supervision and administration of the Sponsored Research.

1.13 "**Related Intellectual Property**" means all inventions, whether patentable or not, that are (a) conceived (as determined by United States patent law) in the conduct of the Sponsored Research during the Term, and (b) during the Term either (i) reduced to practice (as determined by United States patent law) in the conduct of the Sponsored Research, or (ii) disclosed to Penn's Penn Center for Innovation on an invention disclosure form, and (c) that are related to or have applicability in connection with the development and research of [***], including, in each case, all United States and foreign patent applications claiming said patentable inventions, including any divisional, continuation, continuation-in-part (to the extent that the claims are directed to said patentable inventions), and foreign equivalents thereof, as well as any patents issued thereon or reissues or reexaminations thereof. For clarity, Related Intellectual Property also includes all significant copyrights and copyrightable software created in the conduct of the Sponsored Research during the term of this Agreement and that have applicability in connection with the development and research of [***].

1.14 "**Penn mRNA Information**" means any know-how, materials, technical information, data, methods and other information that is (a) necessary or useful for the research, development, manufacturing, commercialization, application, use or practice, as applicable, of Penn Intellectual Property or any [***], (b) not any construct directed against CD 19, (c) emergent from performance of the Sponsored Research in the laboratory of Dr. Drew Weissman, (d) controlled by Penn, and (e) identified and clearly documented in a discrete written form.

1.15 "**Research Results**" means all data and information which are generated in the performance of the Sponsored Research during the term of this Agreement. Research Results expressly excludes Penn Intellectual Property.

1.16 "**Sponsored Research**" means the research program described in Attachment A to this Agreement.

1.17 "**Unrelated Intellectual Property**" means all inventions, whether patentable or not, that are (a) conceived (as determined by United States patent law) in the conduct of the Sponsored Research during the Term, and (b) during the Term either (i) reduced to practice (as determined by United States patent law) in the conduct of the Sponsored Research or (ii) disclosed to Penn's Penn Center for Innovation on an invention disclosure form, and that are not a) Related Intellectual Property or b) an invention directed against CD 19, including all United States and foreign patent applications claiming said patentable inventions, including any divisional, continuation, continuation-in-part (to the extent that the claims are directed to said patentable inventions), and foreign equivalents thereof, as well as any patents issued thereon or reissues or reexaminations thereof.

1.18 **Other Terms**. The definition of each of the following terms is set forth in the section of the Agreement indicated below.

Defined Term	Section
Agreement	Preamble
Confidential Information	6.1
Effective Date	Preamble
First Refusal Period	5.6.3
Future CAAR Target	5.6.3
Option Exercise Notice	5.6.1
Option Period	5.6.1
Negotiation Period	5.6.1
Party or Parties	Preamble
Penn	Preamble
Penn Indemnitees	8.2
Sponsor	Preamble

ARTICLE 2
SPONSORED RESEARCH

2.1 **Conduct**. Penn shall commence the Sponsored Research after the Effective Date of this Agreement and upon payment by Sponsor of any funds owed, and shall conduct such Sponsored Research in accordance with the terms and conditions of this Agreement. Sponsor acknowledges that Penn and the Principal Investigator shall have the freedom to conduct and supervise the Sponsored Research in a manner consistent with Penn's educational and research missions.

2.2 **Principal Investigator**. If the services of the Principal Investigator become unavailable to Penn for any reason, Penn shall be entitled to designate another member of its faculty who is acceptable to Sponsor to serve as the Principal Investigator of the Sponsored Research. If a substitute Principal Investigator has not been designated within [***] after the original Principal Investigator ceases his or her services under this Agreement, either Party may terminate this Agreement upon written notice thereof to the other Party, subject to the provisions of ARTICLE 7.

ARTICLE 3
REIMBURSEMENT OF COSTS & PAYMENT

3.1 **Reimbursement**. Sponsor shall reimburse Penn for an amount equal to its expenditures and reasonable overhead incurred in the conduct of the Sponsored Research in an amount not to exceed the total amount of [***] as set forth in Attachment A. Sponsor acknowledges that this amount is a good faith estimate only and not a guarantee of the cost to conduct the Sponsored Research. If at

any time Penn determines that it will require additional funds for the Sponsored Research, it shall notify Sponsor and provide an estimate of the additional amount. Sponsor shall not be liable for any costs in excess of the amount of [***] unless it has agreed in writing to provide additional funds. All amounts provided by Sponsor shall be used only for the Sponsored Research.

3.2 **Payment**. Sponsor shall make payments in advance to Penn in accordance with the payment schedule set forth in Attachment A. All payments shall clearly identify the Principal Investigator, Penn ERA Number [***], and the term "sponsored research". All payments are to be payable in United States dollars, and if by check, made out to "The Trustees of the University of Pennsylvania", and sent to:

[***]For all payments made by wire transfer (preferred for sponsored research agreements), banking information is as follows:

Banking Information:

Bank Name:	[***]
Bank Address:	[***]
ACH Coordinator:	[***]
Account Title:	[***]
Account Type:	[***]
Account #:	[***]
ABA Routing #:	[***]
SWIFT CODE:	[***]
CHIPS:	[***]
Reference:	[***]

3.3 **Equipment**. Title to any equipment, laboratory animals, or any other materials made or acquired with funds provided under this Agreement shall vest in Penn, and such equipment, animals, or materials shall remain the property of Penn following termination of this Agreement.

ARTICLE 4
RESEARCH RESULTS; RECORDS AND REPORTS

4.1 **Research Results**. Sponsor shall have the right to use Research Results disclosed to Sponsor in records and reports for any lawful purpose subject to the limitations in Section 6.3. Sponsor shall need to obtain a license to use Research Results from Penn if such use would infringe any copyright or any claim of a patent application or issued patent owned by Penn, except to the extent such license is granted pursuant to this Agreement or any other agreement between the Parties.

4.2 **Records**. Principal Investigator shall maintain records of the results of the Sponsored Research and shall provide Sponsor with reports of the progress and results of the Sponsored Research in accordance with Attachment A. Penn shall maintain records of the use of the funds provided by Sponsor and no later than [***] following the end of each calendar quarter, shall provide to Sponsor a summary report of the use of such funds during such calendar quarter.

4.3 **Research Reports**. Penn hereby grants Sponsor a royalty-free, nontransferable, non-exclusive right to copy, reproduce and distribute any research reports furnished to Sponsor under this Agreement, or any excerpts or portions thereof, subject to the limitations in Section 6.3. Sponsor may not charge fees for said research reports, use said research reports for advertising or

promotional activities, or alter or modify said research reports (other than creating excerpts or portions thereof) without the prior written permission of Penn.

ARTICLE 5
INTELLECTUAL PROPERTY

5.1 **Penn Intellectual Property**. Penn shall retain all right, title and interest in and to Penn Intellectual Property and any patents, copyrights, software and tangible research materials and other intellectual property related thereto.

5.2 **Disclosure**. Principal Investigator shall provide Penn and Sponsor a written disclosure of any Penn Intellectual Property reasonably considered patentable. After Sponsor has confirmed receipt of such disclosure (which confirmation can be by email and shall be delivered within [***] of Sponsor's receipt of such disclosure), Sponsor shall advise Penn in writing, no later than [***] after such confirmation of receipt of such disclosure, whether it requests Penn to file and prosecute patent applications related to such Penn Intellectual Property. If Sponsor does not request Penn to file and prosecute such patent applications, Penn may proceed with such preparation and prosecution at its own cost and expense, provided that Penn will first notify Sponsor of its intent to do so. Sponsor shall have [***] from Sponsor's confirmed receipt of such notification to notify Penn that it is electing to retain its rights to such Penn Intellectual Property under Section 5.6, and if Sponsor provides such notification, the terms of Section 5.3 shall apply, including Sponsor's obligation to pay patent expenses, as if Sponsor had requested that Penn file and prosecute such patent applications. If Sponsor fails to so notify Penn of such election, then Penn may proceed with such preparation and prosecution at its own cost and expense, and such patent applications shall be excluded from Sponsor's option under Section 6 hereof, provided, however, that upon Sponsor's request, Penn shall update Sponsor on the filing status of any patent applications related to such Penn Intellectual Property.

5.3 **Prosecution**. Except as may otherwise be agreed by the Parties, Penn shall control the preparation and prosecution of all patent applications and the maintenance of all patents related to Penn Intellectual Property. With regard to any patent applications filed at the request and expense of Sponsor, Penn will, through its patent counsel, consult with Sponsor on patent prosecution. The Parties intend that the common interest privilege will apply to such consultation, but in no event shall such consultation be construed to imply that either Party's counsel represents the other Party in connection with such patent filings and/or prosecution. Sponsor shall reimburse Penn within [***] after receipt of invoice for all documented out-of-pocket patent and legal expenses incurred by Penn in connection with the filing and prosecution of the patent applications and maintenance of the patents that Sponsor has requested Penn to prosecute under Section 5.2 hereof, according to the following schedule: (a) for Related Intellectual Property subject to an exclusive option, the Sponsor shall reimburse all patent and legal expenses; (b) for Unrelated Intellectual Property subject to a non-exclusive option, the Sponsor shall reimburse pro-rata with other active commercial licensees or optionees, and [***] of the expenses if there do not exist any other active commercial licensees or optionees, in each case, determined at the time the expenses are incurred. Penn shall provide prompt written notice to Sponsor of the existence of any such commercial licensee or optionee. For the avoidance of doubt, in the event Sponsor does not exercise its option rights under Section 5.6 of this Agreement with respect to any Related Intellectual Property or Unrelated Intellectual Property during the applicable Option Period, or if the Parties are otherwise unable to execute an agreement pursuant to which Sponsor receives a license to any such Related Intellectual Property or Unrelated Intellectual Property during the applicable Negotiation Period, then Sponsor shall have no further obligation to reimburse Penn for any patent and legal expenses

with respect to such Related Intellectual Property or Unrelated Intellectual Property following the expiration of such Option Period or Negotiation Period, as applicable.

5.4 **Software**. Principal Investigator shall provide Penn and Sponsor a written disclosure of any copyrightable software created in the conduct of the Sponsored Research during the term of this Agreement that Principal Investigator reasonably considers to be scientifically valuable, provided that Principal Investigator shall have no obligation to provide the source code for such software.

5.5 **Non-Exclusive Internal Research License**. Penn hereby grants to Sponsor a non-transferable (except as set forth in Section 9.7), non-exclusive license to use the Penn Intellectual Property for internal research purposes only for research of [***] in the Field of Use for a period beginning on the Effective Date and ending [***] following the expiration or earlier termination of this Agreement.

5.6 **Options**.

5.6.1 **Related Intellectual Property** [***]. In consideration of Sponsor's funding of the Sponsored Research and payment for intellectual property expenses as provided for in Section 5.3, Penn grants Sponsor a first exclusive option to negotiate to acquire a worldwide exclusive license, [***]with the right to sublicense through up to [***]tiers, on commercially reasonable terms, under the Related Intellectual Property, to make, have made, use, import, offer for sale and sell [***], in the Field of Use. Any license to Related Intellectual Property for an invention that has not been reduced to practice in the conduct of the Sponsored Research is contingent upon execution of a subsequent sponsored research agreement with Sponsor for research to be conducted at Penn for reduction to practice of such invention. Any license to [***]Products shall be limited to their use solely in conjunction with either or both of [***]. The Parties shall negotiate and incorporate into the License Agreement mutually agreeable and commercially reasonable financial terms and diligence milestones specific to the development of [***], or alternatively, negotiate and enter into a separate license agreement. These diligence milestones shall take into account the stage of research and potential scientific challenges of the applicable [***] and reasonably expected timelines for achievement of such milestones.

If Sponsor fails to exercise its option to negotiate a license to any Related Intellectual Property prior to [***] after transmittal of the final report as set forth on Attachment A (the "**Option Period**"), or if Sponsor fails to make payment for intellectual property expenses as provided for in Section 5.3 with respect to such Related Intellectual Property, Penn shall be free to license such Related Intellectual Property to any party upon such terms as Penn deems appropriate, without any further obligation to Sponsor. Sponsor shall notify Penn in writing within the Option Period if it intends to exercise such option (the "**Option Exercise Notice**"). In the event Sponsor exercises such option, the Parties will negotiate appropriate financial and diligence terms in good faith for a period of [***] following the Option Exercise Notice (the "**Negotiation Period**"). If the Parties come to agreement on such terms, then such terms shall be reflected in a license agreement executed by the Parties, or alternatively, (1) such patent application(s) or patent(s) in the Related Intellectual Property shall be included as appropriate in the License Agreement, (2) the financial and diligence terms of Exhibit B of the License Agreement shall be amended, and (3) as to each patent application that is Related Intellectual Property for which Sponsor has exercised its option, Sponsor shall amongst other consideration pay Penn an upfront fee to be negotiated by the Parties. Prior to, and during the Option Period and Negotiation Period, Penn shall not assign, transfer, convey, or grant any rights in or otherwise encumber such

Related Intellectual Property in any manner that would impair Sponsor's rights in and to such Related Intellectual Property under this Agreement.

5.6.2 [***]**Unrelated Intellectual Property**. In further consideration of Sponsor's funding of the Sponsored Research and payment for intellectual property expenses as provided for in Section 5.3, Penn grants Sponsor a first option during the Option Period to negotiate to acquire a non-exclusive worldwide license, with the right to sublicense through up to [***]tiers, on commercially reasonable terms, under the Unrelated Intellectual Property and [***], to make, have made, use, import, offer for sale and sell [***], in the Field of Use. Any license to Unrelated Intellectual Property for an invention that has not been reduced to practice in the conduct of the Sponsored Research is contingent upon execution of a subsequent sponsored research agreement with Sponsor for research to be conducted at Penn for reduction to practice of such invention. Notwithstanding the foregoing, [***] Information may only be sublicensed in combination with Penn Intellectual Property for manufacturing, development, or sale of a [***] in the Field of Use. If Sponsor fails to exercise its option within the Option Period, or if Sponsor fails to make payment for intellectual property expenses as provided for in Section 5.3, Penn shall be free to license such Unrelated Intellectual Property to any party upon such terms as Penn deems appropriate, without any further obligation to Sponsor. Sponsor shall provide Penn with an Option Exercise Notice within the Option Period if it intends to exercise such option. In the event Sponsor exercises such option, the Parties will negotiate the terms of a license agreement with respect to such Unrelated Intellectual Property in good faith during the Negotiation Period. Prior to, and during the Option Period and the Negotiation Period, Penn shall not assign, transfer, convey, or grant any rights in or otherwise encumber such Unrelated Intellectual Property in any manner that would impair Sponsor's option to Unrelated Intellectual Property under this Agreement.

5.6.3 **Prospective Intellectual Property -** [***]. Provided that (a) the Parties execute a prospective sponsored research agreement for research to be conducted at Penn in the field of [***] within [***] of the Effective Date, and (b) Sponsor agrees to provide payment for associated prospective Penn intellectual property expenses as they arise during the term of such future sponsored research agreement, Penn shall grant Sponsor an option to negotiate to acquire worldwide licenses, with the right to sublicense through up to [***]tiers, on commercially reasonable terms to Penn patent rights in the field of [***] controlled by Penn that are (x) conceived under the prospective sponsored research agreement, and (y) either (i) reduced to practice (as determined by United States patent law) under the prospective sponsored research agreement or (ii) disclosed to Penn's Penn Center for Innovation on an invention disclosure form, to make, have made, use, import, offer for sale and sell [***] that use or incorporate targets selected from [***] to be developed under the prospective sponsored research program, within the Field of Use. Any such license to Penn patent rights in the field of [***]based on an invention that has not been reduced to practice is contingent upon execution of a subsequent sponsored research agreement with Sponsor for research to be conducted at Penn for reduction to practice of such invention. Any such license shall stipulate that [***] shall be used solely in conjunction with either of the [***]categories. In the event that Penn receives an offer from a third party to support research in the Weissman laboratory for a [***] during the time period running for [***] after the Effective Date, Sponsor shall have a [***] first right of first refusal ("**First Refusal Period**") to sponsor this [***]research, on an individual [***] basis. Provided that a) Sponsor elects not to fund such Future CAAR Target during a First Refusal Period or b) the [***] period after the Effective Date expires, Penn may partner any [***] program not subject to a sponsored research agreement with Sponsor with any other party with no further obligations to Sponsor.

5.7 **Retained Rights and Government Rights**. Any license granted to Sponsor pursuant to Section 5.5 and 5.6 hereof shall be subject to Penn's right to use and permit other nonprofit organizations to use Penn Intellectual Property for educational, research and patient care purposes, and if applicable, to the rights of the United States government reserved under Public Laws 96-517, 97-256 and 98-620, codified at 35 U.S.C. 200-212, and any regulations issued thereunder. Notwithstanding the foregoing, any license granted to Sponsor pursuant to Section 5.5 or 5.6 shall not include retained rights that extend to Penn's patient care purposes by the Weissman laboratory for any Product during the time period when such Product is in active clinical development by Sponsor and ending upon marketing approval of such Product, to the extent Sponsor has provided details of such Product to Penn in writing prior to IND filing for such Product.

ARTICLE 6
CONFIDENTIALITY & PUBLICATION

6.1 **Confidential Information**. Sponsor does not intend to disclose confidential information to Penn unless it is necessary to or useful for the performance of the Sponsored Research. Notwithstanding the foregoing, Sponsor may provide Penn with scientific, technical, business, or other information which is treated by Sponsor as confidential or proprietary ("**Confidential Information**"). Any Confidential Information provided by Sponsor will be in writing and clearly marked by Sponsor as "Confidential" or, if disclosed orally, written notice of the confidential nature thereof will be provided within [***] of disclosure. Penn shall protect Sponsor's Confidential Information with the same degree of care as Penn's own confidential information. Penn shall not use Confidential Information for any purpose other than in connection with performing the Sponsored Research, and shall not disclose Confidential Information to any third party without Sponsor's prior written consent. The Confidential Information provided to Penn by Sponsor will remain the property of the Sponsor, and will be disclosed by Penn only to those persons necessary for the performance of this Agreement who are under obligations of confidentiality substantially similar to those contained herein. Penn's and the Principal Investigator's obligations of confidentiality will exist during the performance of this Agreement and for [***] following termination or expiration of this Agreement, unless disclosure is required by law or regulation.

The confidentiality obligations contained herein shall not apply to Confidential Information that is:

i. Known by Penn or Principal Investigator without restriction prior to disclosure under this Agreement;

ii. Disclosed to Penn or Principal Investigator by a third party without an obligation of confidentiality;

iii. Available to the public not through a breach of this Agreement by Penn or Principal Investigator;

iv. Independently developed by Penn or Principal Investigator without knowledge or use of, or reference to, Confidential Information disclosed by Sponsor under this Agreement as evidenced by Penn's written records; or

v. Published or disclosed in accordance with the terms of this Agreement.

6.2 **Disclosure Required by Court Order or Law**. If Penn is required to disclose Confidential Information, or any terms of the Agreement, pursuant to the valid order or requirement of a court, administrative agency, or other governmental body or applicable law, Penn may disclose such

Confidential Information or terms to the extent required, provided, however, that Penn promptly provides to the Sponsor with prior written notice (to the extent legally permissible) of such disclosure and Sponsor may attempt to obtain an order or other remedy protecting the Confidential Information from public disclosure. To the extent that Confidential Information so disclosed does not become part of the public domain by virtue of such disclosure, it shall remain Confidential Information protected pursuant to Section 6.1.

6.3 **Penn Intellectual Property**. In order to preserve the patentability of Penn Intellectual Property and to preserve Penn's publication rights, Sponsor shall maintain Penn Intellectual Property, Research Results and information provided pursuant to the Sponsored Research (whether oral or written) as confidential and shall not disclose such information to any third party until the publication of such information by the Principal Investigator or until Penn provides Sponsor with written verification that all desirable patentable inventions have been protected, whichever occurs sooner, provided, however, that Sponsor may disclose such information to actual or potential investors, acquirers, partners, collaborators, licensees, or sub-licensees without Penn's prior written consent, provided such third parties are subject to written confidentiality obligations substantially similar to those contained herein. Sponsor's obligations of confidentiality will exist during the term of this Agreement and for [***] following the termination or expiration of this Agreement, unless disclosure is required by law or regulation.

Sponsor shall have the right to disclose any of the information described above to the extent required pursuant to the valid order or requirement of a court, administrative agency, or other governmental body or applicable law, subject to the terms and obligations set forth in Section 6.2, *mutatis mutandis.* The confidentiality obligations contained in this Section 6.3 shall not apply to any information that is subject to any of the clauses (i) through (v) of Section 6.1, *mutatis mutandis.*

Penn shall maintain Penn Intellectual Property and Research Results as confidential and shall not disclose such information to any third party until the publication or presentation of such information by the Principal Investigator pursuant to the terms of this Agreement, provided, however, that (a) Research Results and Penn Intellectual Property shall not be considered Confidential Information for purposes of publication in accordance with Section 6.4 below, (b) Penn shall be permitted to disclose Penn Intellectual Property and Research Results in patent applications and related documents, (c) Penn may disclose Penn Intellectual Property in the event Sponsor does not exercise its option to such Penn Intellectual Property under Section 5.5 above or a license agreement, including the License Agreement, is not entered into with respect to such Penn Intellectual Property, and (d) Penn may use and disclose Research Results for educational and noncommercial research purposes. Penn's obligations of confidentiality under this paragraph will exist during the term of this Agreement and for the earlier of (i) [***] following the termination or expiration of this Agreement or (ii) the publication or presentation of such Research Results, unless disclosure is required by law or regulation.

6.4 **Publications**. Penn shall have the first right to publish or present Research Results or other information and material resulting from the Sponsored Research. Penn shall furnish the Sponsor with a copy of any proposed publication or presentation at least [***] in advance of the date of such presentation or the submission of said proposed publication in order for Sponsor to review and comment on said proposed publication or presentation to (a) determine whether such contains any Confidential Information and (b) enable Sponsor to identity any Penn Intellectual Property that it wishes Penn to file patent applications on or to seek other intellectual property protection for. If within the [***]review period (i) Sponsor notifies Penn that the Sponsor requires deletion from the publication or presentation of Sponsor Confidential Information, the Parties will cooperate to modify the disclosure to ensure Sponsor Confidential Information is not disclosed or (ii) if Sponsor

requests that publication or presentation be delayed to allow for patent filings or other intellectual property protection on certain items in the proposed publication or presentation, Penn shall delay the publication or presentation for up to [***] to allow for the filing of patent applications or other intellectual property protection.

ARTICLE 7
TERM & TERMINATION

7.1 **Term**. The initial term of this Agreement shall begin on the Effective Date of this Agreement and shall end on the [***] of the Effective Date unless terminated sooner pursuant to Sections 2.2 or 7.2 hereof (the "Term"). This Agreement may be extended or renewed only by mutual written agreement executed by duly authorized representatives of the Parties.

7.2 **Termination**. In addition to the termination right set forth in Section 2.2 hereof,

i. either Party may terminate this Agreement effective upon written notice to the other Party, if the other Party breaches any of the terms or conditions of this Agreement and fails to cure such breach within [***] after receiving written notice thereof. In the event of an incurable breach, the non-breaching Party may terminate this Agreement effective immediately upon written notice to the breaching Party; or

ii. Sponsor may terminate this Agreement in its entirety, or on an [***], for any or no reason effective upon [***] written notice to Penn. For clarity, cessation or truncation of a sub-project pertaining to an individual [***] shall not be deemed termination of the Agreement.

7.3 **Effects of Termination**.

i. Any early termination of the Agreement shall result in automatic cross-termination of the Background IP Option Agreement with immediate effect. For clarity, any termination of this Agreement following Sponsor's full payment to Penn of the initially agreed-upon budget of [***] shall not be considered early termination of the Agreement for purposes of this Section 7.3(i).

ii. In the event of termination of this Agreement prior to its stated term whether for breach or for any other reason whatsoever, Penn shall be entitled to payment for the work in progress up to the date of termination, and for allowable costs, to the extent contemplated in the budget included in Attachment A. Allowable costs include, without limitation, [***]. In the event of termination, or upon expiration of this Agreement, Penn shall submit a final report of all costs incurred and all funds received under this Agreement within [***] after the effective termination or expiration date. The report shall be accompanied by a check in the amount of any excess of funds advanced over costs and allowable commitments incurred. In case of a deficit of funds, Sponsor shall pay Penn the amount needed to cover costs and allowable commitments incurred by Penn under this Agreement (for clarity, to the extent such costs and commitments are included in the budget).

iii. Termination or expiration of this Agreement shall not affect the rights and obligations of the Parties accrued prior to termination hereof. The provisions of ARTICLE 3; ARTICLE 4; ARTICLE 5; ARTICLE 6; ARTICLE 7; ARTICLE 8; and ARTICLE 9, shall survive such termination or expiration.

ARTICLE 8

DISCLAIMER OF WARRANTIES, INDEMNIFICATION

8.1 PENN MAKES NO WARRANTIES, EXPRESS OR IMPLIED, AS TO ANY MATTER WHATSOEVER, INCLUDING, WITHOUT LIMITATION, WARRANTIES WITH RESPECT TO THE CONDUCT, COMPLETION, SUCCESS OR PARTICULAR RESULTS OF THE SPONSORED RESEARCH, OR THE CONDITION, OWNERSHIP, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE OF THE SPONSORED RESEARCH OR ANY PENN INTELLECTUAL PROPERTY OR RESEARCH RESULTS OR THAT USE OF PENN INTELLECTUAL PROPERTY OR RESEARCH RESULTS WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK OR OTHER INTELLECTUAL PROPERTY RIGHT OF A THIRD PARTY. EXCEPT IN THE CASE OF PENN'S GROSS NEGLIGENCE OR WILLFUL MISCONDUCT, PENN SHALL NOT BE LIABLE FOR ANY DIRECT, INDIRECT, CONSEQUENTIAL, PUNITIVE OR OTHER DAMAGES SUFFERED BY SPONSOR OR ANY OTHER PERSON RESULTING FROM THE SPONSORED RESEARCH OR SPONSOR'S USE OF ANY PENN INTELLECTUAL PROPERTY, ANY RESEARCH RESULTS OR ANY PRODUCTS RESULTING THEREFROM. EXCEPT IN THE CASE OF SPONSOR'S GROSS NEGLIGENCE OR WILLFUL MISCONDUCT, SPONSOR SHALL NOT BE LIABLE FOR ANY INDIRECT. CONSEQUENTIAL OR PUNITIVE DAMAGES SUFFERED BY PENN RESULTING FROM THE SPONSORED RESEARCH OR PENN'S USE OF ANY PENN INTELLECTUAL PROPERTY, ANY RESEARCH RESULTS OR ANY PRODUCTS RESULTING THEREFROM; PROVIDED, THAT, FOR THE AVOIDANCE OF DOUBT, THIS SECTION 8.1 SHALL NOT BE INTERPRETED TO AFFECT OR LIMIT SPONSOR'S INDEMNIFICATION OBLIGATION UNDER SECTION 8.2 BELOW.

8.2 **Indemnification**.

Sponsor shall indemnify, defend and hold harmless Penn and its respective trustees, officers, faculty, students, employees, contractors and agents (the "**Penn Indemnitees**") from and against any and all liability, damage, loss, cost or expense (including reasonable attorneys' fees), which the Penn Indemnitees may hereafter incur, or be required to pay as a result of Sponsor's use of any Penn Intellectual Property or Research Results or as a result of any breach of this Agreement or any act or omission of Sponsor, its employees, affiliates, contractors, licensees or agents, provided that Sponsor's obligations pursuant to this Section 8.2 shall not apply to the extent such claims or suits result from the negligence or willful misconduct of any of Penn Indemnitees or any breach of this Agreement by Penn, each as determined by a court of law.

As a condition to a Penn Indemnitee's right to receive indemnification under this Section 8.2, Penn shall: (a) promptly notify Sponsor when it becomes aware of a claim or suit for which indemnification may be sought pursuant hereto; (b) cooperate with Sponsor in the defense, settlement or compromise of such claim or suit; and (c) permit the Sponsor to control the defense, settlement or compromise of such claim or suit, including the right to select defense counsel. In no event, however, may Sponsor compromise or settle any claim or suit in a manner which (a) admits fault or negligence on the part of Penn or any other Penn Indemnitee; or (b) commits Penn or any other Penn Indemnitee to take, or forbear to take, any action, without the prior written consent of Penn. Penn shall reasonably cooperate with Sponsor and its counsel in the course of the defense of any such suit, claim or demand.

ARTICLE 9
ADDITIONAL PROVISIONS

9.1 **Force Majeure**. Neither Party shall be liable for any failure to perform as required by this Agreement to the extent such failure to perform is due to circumstances reasonably beyond such Party's control, including, without limitation, labor disturbances or labor disputes of any kind, accidents, failure of any governmental approval required for full performance, civil disorders or commotions, terrorism, acts of aggression, acts of God, unforeseeable and irresistible energy or other conservation measures imposed by law or regulations, explosions, failure of utilities, material shortages, disease, or other such occurrences.

9.2 **Relationship of the Parties**. Nothing in this Agreement is intended or shall be deemed, for financial, tax, legal or other purposes, to constitute a partnership, agency, joint venture or employer-employee relationship between the Parties. The Parties are independent contractors and at no time will either Party make commitments or incur any charges or expenses for or on behalf of the other Party.

9.3 **Expenses**. Except as otherwise provided in this Agreement, each Party shall pay its own expenses and costs incidental to the preparation of this Agreement and to the consummation of the transactions contemplated hereby

9.4 **Third Party Beneficiary**. No party, other than Penn or Sponsor shall be entitled to any rights whatsoever by virtue of the relationships created by or arising under this Agreement, including, without limitation, rights as a third party beneficiary

9.5 **Use of Names**. Except as set forth in the License Agreement, Sponsor and its affiliates may not use the name, logo, seal, trademark, or service mark (including any adaptation of them) of Penn or any Penn school, organization, employee, student or representative, without the prior written consent of Penn. Notwithstanding the foregoing, Sponsor may use the name of Penn and the Principal Investigator and other Penn employees directly supported by Sponsored Research funds as identified in the budget set forth in Attachment A in a non-misleading and factual manner solely to state Sponsor's funding of this Sponsored Research. Except as set forth in the License Agreement, Penn shall not use Sponsor's name without Sponsor's prior written consent except that Penn may acknowledge Sponsor's funding of this Sponsored Research and any scientific contributions in scientific publications, in listings of sponsored research projects and for other academic purposes.

9.6 **No Discrimination**. Neither Penn nor Sponsor will discriminate against any employee or applicant for employment because of race, color, sex, sexual or affectional preference, age, religion, national or ethnic origin, handicap, or veteran status.

9.7 **Successors and Assignment**.

The terms and provisions hereof shall inure to the benefit of, and be binding upon, the Parties and their respective successors and permitted assigns.

Sponsor may not assign or transfer this Agreement or any of Sponsor's rights or obligations created hereunder, by operation of law or otherwise, without the prior written consent of Penn. Notwithstanding the foregoing, Sponsor may assign its rights and obligations under this Agreement without the prior written consent of Penn to a successor in connection with the merger, consolidation, reorganization or sale of all or substantially all of its assets or its business; provided,

that (I) there exists no material breach by Sponsor of any material term of this Agreement, (II) Sponsor provides prompt written notice of the transaction to Penn, and (III) the assignee agrees in writing to be legally bound by this Agreement. Any permitted assignment will not relieve Sponsor of any obligation of Sponsor that has accrued at the time of the assignment.

Any assignment not in accordance with this Section 9.7 shall be void.

9.8 **Further Actions**. Each Party agrees to execute, acknowledge and deliver such further instruments and to do all such other acts as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

9.9 **Entire Agreement of the Parties; Amendments** . This Agreement and the Schedules and Attachments hereto, the Background IP Option Agreement, constitute and contain the entire understanding and agreement of the Parties respecting the subject matter hereof and cancel and supersede any and all prior negotiations, correspondence, understandings and agreements between the Parties, whether oral or written, regarding such subject matter. No waiver, modification or amendment of any provision of this Agreement shall be valid or effective unless made in a writing referencing this Agreement and signed by a duly authorized officer of each Party.

9.10 **Governing Law**. This Agreement shall be governed by and interpreted in accordance with the laws of the Commonwealth of Pennsylvania, excluding application of any conflict of laws principles that would require application of the law of a jurisdiction outside of the Commonwealth of Pennsylvania.

9.11 **Dispute Resolution**. If a dispute arises between the Parties concerning this Agreement, then the Parties will confer, as soon as practicable, in an attempt to resolve the dispute. If the Parties are unable to resolve such dispute amicably, then the Parties will submit to the exclusive jurisdiction of, and venue in, the state and Federal courts located in the Eastern District of Pennsylvania.

9.12 **Notices and Deliveries**. Any notice, request, approval or consent required or permitted to be given under this Agreement shall be in writing and directed to a Party at its address shown below or such other address as such Party shall have last given by notice to the other Party. A notice will be deemed received: if delivered personally, on the date of delivery; if mailed, [***] after deposit in the United States mail; if sent via courier, [***] after deposit with the courier service.

For Penn

[***]

with a copy to:

[***]

For Sponsor:

[***]

with a copy to:

[***]

9.13 **Waiver**. A waiver by either Party of any of the terms and conditions of this Agreement in any instance shall not be deemed or construed to be a waiver of such term or condition for the future, or of any other term or condition hereof. All rights, remedies, undertakings, obligations and agreements contained in this Agreement shall be cumulative and none of them shall be in limitation of any other remedy, right, undertaking, obligation or agreement of either Party.

9.14 **Severability**. When possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under law, but if any provision of this Agreement is held to be prohibited by or invalid under law, such provision will be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of this Agreement. The Parties shall make a good faith effort to replace the invalid or unenforceable provision with a valid one which in its economic effect is most consistent with the invalid or unenforceable provision.

9.15 **Interpretation**. The words "include," "includes" and "including" shall be deemed to be followed by the phrase "without limitation." All references herein to Articles, Sections, and Schedules shall be deemed references to Articles and Sections of, and Schedules to, this Agreement unless the context shall otherwise require.

9.16 **Counterparts**. This Agreement may be executed in counterparts, each of which will be deemed an original, and all of which together will be deemed to be one and the same instrument. A portable document format (PDF) or electronic copy of this Agreement, including the signature pages, will be deemed an original.

[**SIGNATURE PAGE FOLLOWS**]

IN WITNESS WHEREOF, the duly authorized representatives of the Parties hereby execute this Agreement as of the date first written above.

THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA		**CABALETTA BIO, INC**	
By:	[***]	By:	/s/ Steven Nichtberger
Name:	[***]	Name:	Steven Nichtberger
Title:	[***]	Title:	Chief Executive Officer

I have read and understood the responsibilities of the Principal Investigator:

Signature: /s/ Drew Weissman
Dr. Drew Weissman

Attachment A

Summary of Sponsored Research

Work Scope & Details of Program — See attached Appendix 1 to Attachment A.

Principal Investigator - Drew Weissman, M.D., Ph.D.; [***]

Representative of Sponsor - Steven Nichtberger; [***]

Period of Performance — [***]

Report Schedule — Final report due within [***] after completion of the Sponsored Research.

Interim reports due [***] after commencement of the Sponsored Research.

Budget— See attached Appendix 2 to Attachment A; [***].

Payments under this Agreement will be payable within [***] of Sponsor's receipt of an invoice from Penn.

Payment Schedule —

Date Payment Due	Amount of Payment Due
[***]	[***]
[***]	[***]

APPENDIX 1 TO ATTACHMENT A

WORK SCOPE & DETAILS OF PROGRAM

[***]

APPENDIX 2 TO ATTACHMENT A

BUDGET

[***]

CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND REPLACED WITH "[***]". SUCH IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS (I) NOT MATERIAL AND (II) THE TYPE OF INFORMATION THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

University *of* Pennsylvania

Option Agreement

Signature Page

Company Information	
Company's full legal name and address: *Cabaletta Bio, Inc.* *2929 Arch Street, Suite 600* *Philadelphia, PA 19104*	*Company primary phone number:* 267-759-3100 *Company primary fax number:*

Penn Information		
Notice Address:	***Payment Address:***	
[***]	**By ACH/Wire:** [***]	**By Check (lockbox):** [***]

Patent Rights	
Penn Dockets and Descriptions: *See Attachment A*	Field of Use: *"Field of Use'* means the following subfields (each a "Subfield"): [***].
	Licensed Product: *"Licensed Product"* means [***]

Payment Terms
Option Fee: $[***]

Term	
Effective Date: The effective date of SRA (as defined in Section 2)	*Initial Term:* Until [***].

Signatures	
This Agreement includes this Signature Page and all of the attached Terms and Conditions. By signing below, Company and Penn agree to all of the provisions.	
Cabaletta Bio, Inc.	**The Trustees of the University of Pennsylvania**
By: /s/ Steven NichtbergerDate: December 23, 2021 *(please sign)* Name: Steven Nichtberger, MD Title: CEO	By: [***] Date: December 23, 2021 *(please sign)* Name: [***]Title: [***]

Option Agreement

Terms and Conditions

1. **Option Grant.** Penn grants to Company a first option, during the Term, to negotiate to acquire a non-exclusive worldwide license, with the right to sublicense through up to [***]tiers, to make, have made, use, import, offer for sale and sell Licensed Products using or incorporating Patent Rights in the Field of Use (the "*Option").* The term "Patent *Rights'* means (a) all of Penn's patent rights represented by or issuing from the Penn dockets listed on the Signature Page, (b) any continuations, provisionals, continued prosecution applications, substitutions, extensions and term restorations, registrations, confirmations, reexaminations, renewals, divisional and re-issue applications thereof, but excluding continuations-in-part except to the extent of claims entirely supported in the specification and entitled to the priority date of the parent application, and (c) any corresponding foreign counterparts and any extensions to the foregoing. No other rights and no licenses are granted.

2. **License Negotiations.** During the Term, but only following execution of the SRA, Company shall notify Penn in writing if it intends to exercise the option set forth in Section 1 above. In the event Company exercises such option, Company and Penn will negotiate in good faith the terms and conditions of a definitive Patent License Agreement for the Patent Rights for a period of [***]and [***] thereafter (the "Negotiation *Period"*). During [***], Penn will not enter into any negotiations with any third party regarding an exclusive commercial license under the Patent Rights for use with or incorporation into Licensed Products in the Field of Use that would conflict with the option rights granted to Company hereunder. "SRA" means a sponsored research agreement between Company and Penn for mRNA-LNP research involving CAARs to be conducted in the Weissman Lab at Penn and executed by the parties concurrently with this Agreement. Under the SRA, Company shall provide committed funding to Penn's Weissman Lab of at least $[***] for development of products and services related to the Patent Rights in the Field of Use.

3. **Minimum Terms.** Any Patent License Agreement negotiated pursuant to this Agreement will be based upon Penn's standard Patent License Agreement, or if deemed applicable by the parties, the Cabaletta Amended and Restated License Agreement dated effective July 23, 2019 by and among Penn, CHOP, and Company, as amended by its First Amendment dated May 1, 2020 and its Second Amendment dated October 19, 2021. Any license will be subject to any applicable rights retained by the US government in intellectual property funded by a Federal agency. In any license, Penn will reserve the right to use, and to allow other non-commercial entities to use, the Patent Rights for educational, research and patient care purposes.

4. **Option Fee.** On the Effective Date, Company will pay to Penn the non-refundable and non-creditable Option Fee.

5. **Expiration.** This Agreement will expire automatically at the end of the Term unless otherwise agreed upon by both parties in writing.

6. **Early Termination.** This Agreement will terminate before the expiration of the Term: (a) upon the written agreement of both parties to such termination, or (b) upon [***] prior written notice by Company of its intention to terminate at any time, or (c) immediately upon early termination of the associated SRA.

7. **Effect of Expiration or Termination.** Upon the expiration or termination of this Agreement for any reason (except for termination upon execution of a definitive Patent License Agreement, and only following the Negotiation Period if applicable): Penn may exclusively license the Patent Rights in the Field of Use to any third party at any time and upon any terms without further obligation to Company. The terms and conditions of Paragraphs 7, 11, 12, 13 and 14 will survive in accordance with their respective terms. If Company has exercised its option during the Term, then Company's rights to negotiate a license as set forth in Section 2 shall survive such expiration for the time period set forth in such Section 2.

8. **Intentionally Omitted**

9. **Payment Terms.** All payments are payable to "The Trustees of the University of Pennsylvania" at the payment addresses shown on the Signature Page. All payments will be in United States Dollars.

10. **Patent Maintenance.** Except as may otherwise be agreed by the parties, in a definitive Patent License Agreement or otherwise, Penn will control, prosecute and maintain the Patent Rights during the Term. During the Term, Penn will, use reasonable efforts to inform Company, through its patent counsel, material patent prosecution decisions that are pending related to the Patent Rights, and will reasonably consider Company's input on such decisions.

11. **Patent Expenses.** Company will reimburse Penn for all patent and legal expenses incurred by Penn during the Term with respect to the Patent Rights at the rate of (a) [***] of the expenses if there are no other active commercial licensees or optionees, and (b) [***] with other active commercial licensees or optionees, in each case determined at the time the expenses are incurred. Penn shall promptly inform Company of the number of any such active commercial licensees or optionees. If Company does not reimburse any such expenses then Penn may proceed with such patent action at its own cost and expense and any patent rights associated with such patent action will be automatically excluded from the term "*Patent Rights"'* and Company's option under Paragraph 1.

12. **Penn's Name.** Company will not use Penn's name or trademarks or the name of any Penn employee in any manner without Penn's prior written consent. Notwithstanding the foregoing, Company may use the name of Penn in a non-misleading and factual manner solely to state that Company has entered into this Option Agreement and been granted the Option. Penn will not use Company's name or trademarks without the prior written consent of Company except that Penn may use the name of Company in a non-misleading and factual manner solely to state that Penn has entered into this Option Agreement and granted the Option to Company.

13. **Disclaimer.** PENN MAKES NO REPRESENTATIONS OR WARRANTIES, EXPRESS OR IMPLIED, INCLUDING BUT NOT LIMITED TO ANY WARRANTY OF PERFORMANCE, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, COMMERCIAL UTILITY, NON-INFRINGEMENT OR TITLE.

14. **Miscellaneous.** Any notice must be in writing and sent to the address of the party listed on the Signature Page. This Agreement may only be modified by a written amendment that is executed by an authorized representative of each party. Any waiver must be express and in writing. No waiver by either party of a breach by the other party will constitute a waiver of any different or succeeding breach. This Agreement will be governed by and construed in accordance with the laws of the Commonwealth of Pennsylvania without regard to conflicts of law principles of any jurisdiction. The parties will use reasonable efforts to resolve amicably any disputes that may relate to or arise under this Agreement. If the parties are unable to resolve the dispute amicably, then the parties will submit to the exclusive jurisdiction of, and venue in, the state and Federal courts located in the Eastern District of Pennsylvania. This Agreement, together with the SRA and any Confidential Disclosure Agreement contain the entire agreement between the parties with respect to subject matter of this Agreement and supersede all other oral or written representations, statements, or agreements with respect to such subject matter. This Agreement is binding upon the parties and their respective heirs, successors, assigns, and personal representatives. Neither party may assign this Agreement without the prior written consent of the other party.

Notwithstanding the foregoing, Company may assign its rights and obligations under this Option Agreement without the prior written consent of Penn to a successor in connection with the merger, consolidation or sale of all or substantially all of its assets or its business, provided, that (i) there exists no material breach by Company of any material term of this Option Agreement, (ii) Company provides prompt written notice of the transaction to Penn, and (iii) the assignee agrees in writing to be legally bound by this Agreement. Any permitted assignment will not relieve Company of any obligation of Company that has accrued at the time of the assignment.

Attachment A

Patents and Patent Applications in Penn Patent Rights

[***]

Exhibit 10.31

CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND REPLACED WITH "[***]". SUCH IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS (I) NOT MATERIAL AND (II) THE TYPE OF INFORMATION THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

OXFORD BIOMEDICA (UK) LIMITED

and

CABALETTA BIO, INC.

LICENCE AND SUPPLY AGREEMENT

Contents

Clause No.		Page No.
1.	Definitions and Interpretation	1
2.	Governance	13
3.	Provision of Services	15
4.	Client Materials	20
5.	Forecasting and Ordering for Batches	21
6.	Delivery and Defective Batches	22
7.	Price and Payment	25
8.	Financial Records and Audit	28
9.	Access to OXB Information	29
10.	Quality Audits and Inspections	29
11.	Regulatory Approvals; Regulatory Matters	30
12.	Intellectual Property	31
13.	Technology Transfer	33
14.	Confidential Information	34
15.	Indemnities and Liability; Insurance	38
16.	Warranties and Representations	41
17.	Duration and Termination	42
18.	General	45

CONFIDENTIAL

THIS AGREEMENT (the "**Agreement**") is made as of the 30th day of December 2021 ("**Effective Date**")

BETWEEN:

(1) **OXFORD BIOMEDICA (UK) LIMITED**, a company incorporated in England and Wales with company registration number 03028927, whose registered office is at Windrush Court, Transport Way, Oxford, OX4 6LT, UK ("**OXB**"); and

(2) **CABALETTA BIO, INC.**, a company incorporated in Delaware whose principal place of business is at 2929 Arch Street, Suite 600, Philadelphia, PA 19104, USA ("**Client**").

BACKGROUND:

(A) OXB has extensive experience in the development and manufacture of therapeutic lentiviral vectors, including manufacturing, process development, product release and analytical technology.

(B) Client wishes to develop and commercialise certain gene therapy products transduced using lentiviral vectors.

(C) OXB and Client entered into the CDA (as defined herein) pursuant to which the Parties evaluated and expanded opportunities to work together.

(D) OXB and Client entered into the FSA (as defined herein) pursuant to which OXB commenced early phase activities for the eventual supply by OXB to Client of cGMP lentiviral vectors targeting Client's gene(s) of interest.

(E) Client now wishes to appoint OXB to manufacture and supply to Client such vectors for clinical purposes.

(F) OXB wishes to grant and Client wishes to accept a licence under OXB's intellectual property rights to develop and commercialise Client's products which incorporate vectors manufactured using OXB's manufacturing process.

(G) Under certain circumstances, OXB wishes to grant and Client wishes to accept the right to have the manufacturing process transferred to Client.

(H) The Parties intend for this Agreement to terminate the CDA and the FSA.

OPERATIVE PROVISIONS

1. Definitions and Interpretation

1.1 **Definitions**. In this Agreement, the following words and expressions shall have the following meanings:

(a) "**Actual Delivery Date**" means the date upon which a Batch is Delivered by OXB;

(b) "**Additional Target Fee**" shall have the meaning given to it in clause 7.2;

(c) "**Additional Target**" means [***] that is agreed by OXB and Client in accordance with clause 2.4;

(d) "**Affiliate**" means any person, firm, trust partnership, corporation, company or other entity or combination thereof which directly or indirectly (i) controls a Party, (ii) is controlled by a Party, or (iii) is under common control with a Party. As used in this definition, the terms "control" and "controlled" will mean ownership of fifty per cent (50%) or more the voting rights of such entity or the power to direct the management of such entity through contract or otherwise;

(e) "**Agreed Delivery Date**" means the date specified in the applicable Scope of Work or Work Order or Change Order by which a Batch will be Delivered by OXB in accordance with clause 6.1;

(f) "**Applicable Law**" means all rules, regulations, laws, statutes, guidelines, judgments and court orders of any kind whatsoever of any Regulatory Authority applicable to a Party's activities hereunder, as amended from time to time, including cGMP of the FDA, the EMA, the European Commission, the ICH guidelines and regulations, and any other regulatory jurisdictions as agreed to in writing by both Parties;

(g) "**Approved Subcontractor**" has the meaning given in clause 3.6;

(h) "**Arising IPR**" means any Intellectual Property Rights prepared, developed, conceived, reduced to practice, generated or derived by or on behalf of either Party in the course of the performance of its obligations under this Agreement;

(i) "**Background IPR**" means information, techniques, Know-How, software, Intellectual Property Rights and materials (regardless of the form or medium in which they are disclosed or stored) that are: (i) owned or Controlled by one Party or its Affiliates prior to the Effective Date or (ii) generated or obtained by a Party independently of the activities conducted in connection with this Agreement and without use of, reliance upon, or reference to the other Party's Confidential Information; and which are provided by such Party to the other for performing this Agreement;

(j) "**Batch**" means a specific quantity of Vector Manufactured by OXB that is intended to have uniform character and quality within specified limits and is produced according to a single cycle of Manufacture, and that is required to be Manufactured in compliance with cGMP as specified in the applicable Scope of Work;

(k) "**Batch Documentation**" means, with respect to a Batch Manufactured by OXB, (1) a copy of the Batch record, (2) the Certificate of Compliance in accordance with the format and subject matter as set out in the Quality Agreement, (3) the Certificate of Analysis, and (4) such other quality related documentation as is required under the Quality Agreement, duly signed by the designated person, corresponding to the Batch;

(l) "**Batch Fee**" means the price payable by Client for a Batch, as set out in Schedule 1 or as otherwise agreed in writing by the Parties under the applicable Scope of Work or Work Order;

(m) "**BLA**" means a biologics license application filed with the FDA to obtain permission to introduce, or deliver for introduction, a biologic product into interstate commerce as provided for under 21 CFR 601.2 or any comparable application filed with the Regulatory Authority of any other country;

(n) "**Business Days**" means any day other than a Saturday or a Sunday on which banks are open for business in both London and Philadelphia;

(o) "**CAAR**" means a chimeric auto antigen receptor;

(p) "**Cancellation Charges**" means the cancellation charges as set out in Schedule 1.

(q) "**CDA**" means the confidentiality agreement between the Parties dated 12 April 2019;

(r) "**cGMP**" mean the then applicable principles and guidelines of current good manufacturing practice and general biologics products standards as contained: (i) in US Federal Food Drug and Cosmetic Act and 21 CFR Chapters 210, 211, 600 and 610; (ii) in EC Directive 2003/94/EC laying down the principles and guidelines of Good Manufacturing Practice in respect of Medicinal Products for Human Use and Investigation Medicinal Products for Human Use; (iii) in EC Directive 2001/20/EC covering the requirements of GMP manufacture for clinical trial usage; (iv) in the European Commission's guidelines "The rules governing medicinal products in the European Union", EudraLex Volume 4, "EU Guidelines to Good Manufacturing Practice - Medicinal Products for Human and Veterinary Use"; (v) in ICH Guidance for Industry Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients; and (vi) in any comparable laws, rules, or regulations of any foreign jurisdiction which may be agreed from time to time between the Parties in writing pursuant to a Scope of Work, Change Order or Work Order, in each case (i) to (vi) as may be amended from time to time;

(s) "**Change Order**" means a document signed by both Parties setting out agreed amendments to Work Packages or termination of Work Packages, and shall include a description of work and detail any changes to the costs of such amended Work Packages and the overall Scope of Work;

(t) "**Claim**" means losses, liabilities, damages, amounts paid in settlement, reasonable legal costs and other reasonable expenses of any nature whatsoever suffered or incurred in connection with any Third-Party demands, claims, actions, or proceedings (whether criminal or civil, in contract, tort or otherwise). For clarity, in connection with any claim for which OXB has an indemnification obligation under clause 15.4(c), "Claim" shall include any reasonable royalties payable to the relevant Third Party;

(u) "**Client Arising IPR**" shall have the meaning set out in clause 12.5;

(v) "**Client Materials**" means the materials identified in the applicable Scope of Work and provided by Client for use in the performance of Services under this Agreement or otherwise deemed to be "Client Materials" herein;

(w) "**Commercial Milestones**" shall have the meaning given to it in Schedule 2;

(x) "**Commercial Milestone Payments**" shall have the meaning given to it in Schedule 2;

(y) "**Commercialise**" or "**Commercialisation**" means any and all activities directed toward marketing, promoting, detailing, distributing, importing, exporting, selling or offering to sell the Licensed Products;

(z) "**Components**" means all raw materials, media, excipients and materials, excluding Client Materials, required for the Manufacture, storage, supply and shipping of Vector in accordance with the Specifications;

(aa) "**Confidential Information**" means all information of a confidential or proprietary nature which is obtained directly or indirectly by one Party (the "**Receiving Party**") or its Affiliates, from the other Party (the "**Disclosing Party**") or its Affiliates at any time during the Term, without regard to the form or manner in which such information is disclosed or obtained (including information disclosed orally or in documentary or electronic form or by way of model, or obtained by observation), and without limiting the foregoing, in addition shall include:

(i) the existence and terms of this Agreement and the FSA, for which both Parties shall be deemed to be a Receiving Party;

(ii) Confidential Information, as such term is defined in the CDA, which information, with effect from the Effective Date, shall be deemed to be Confidential Information of the relevant Party under this Agreement and subject to the terms of this Agreement in place of the terms of the CDA with this Agreement;

(iii) Confidential Information, as such term is defined in the FSA, which information, with effect from the Effective Date, shall be deemed to be Confidential Information of the relevant Party under this Agreement and subject to the terms of this Agreement in place of the terms of the FSA with this Agreement;

(iv) any Know-How within each of OXB's Background IPR or the OXB Arising IPR, for which OXB shall be deemed to be the Disclosing Party and Client the Receiving Party; and

(v) any Know-How within each of Client's Background IPR or the Client Arising IPR for which, in each case, Client shall be deemed to be the Disclosing Party and OXB the Receiving Party;

(bb) "**Control**" or "**Controlled**" means, with respect to any Intellectual Property Right or other intangible property, the possession by a Party (whether by ownership or license, other than a license granted pursuant to this Agreement), of the ability to grant access to, or a license or sublicense of, such rights or property as contemplated under this Agreement;

(cc) "**Cover**", "**Covered**" or "**Covering**" shall mean, with respect to a Patent Right, that, in the absence of a license granted to a person under a Valid Claim included in such Patent Right, the manufacture or use of Vectors or the manufacture, use, research, Development or Commercialisation of Licensed Products would infringe such Valid Claim (or, in the case of a Patent Right that is a patent application, would infringe a Valid Claim in such patent application if it were to issue as a patent);

(dd) "**Defective Batch**" means any Batch that (i) is terminated after the IM Date and before completion, (ii) does not conform to the Specifications, and / or (iii) was not Manufactured in accordance with cGMP, the Quality Agreement or Applicable Law;

(ee) "**Delivery**" of a Batch shall mean the Batch being made available to Client by OXB in accordance with clause 6.1 and Delivered shall be construed accordingly;

(ff) "**Develop**" or "**Development**" means all activities that relate to obtaining, maintaining or expanding Regulatory Approval of a Licensed Product and to supporting appropriate usage for such Licensed Product. This includes: (i) preclinical/nonclinical research and testing, toxicology, and clinical trials; and (ii) preparation, submission, review, and development of data or information for the purpose of submission to a Regulatory Authority to obtain, maintain and/or expand Regulatory Approval of a Licensed Product (including contacts with Regulatory Authorities) and excludes in all cases Commercialisation of Licensed Product;

(gg) "**Development Milestones**" shall have the meaning given to it in Schedule 2;

(hh) "**Development Milestone Payments**" shall have the meaning given to it in Schedule 2;

(ii) "**Development Partner**" means any Affiliate of Client or any Third Party, in each case to whom Client has granted a right or license to research, Develop, or Commercialise the Licensed Products;

(jj) "**EMA**" means the European Medicines Agency and any successor agency thereto;

(kk) "**Facility**" means the facility identified in the Quality Agreement or respective Work Order or approved by Client in writing, which can be:

(i) a OXB manufacturing, laboratory and warehouse facility; and

(ii) the facilities of an Approved Subcontractor;

(ll) "**FDA**" means the United States Food and Drug Administration and any successor agency thereto;

(mm) "**First Commercial Sale**" means, with respect to a given Licensed Product, the first sale to a Third Party (other than an Affiliate or sublicensee) on an arms' length commercial basis of such Licensed Product by a Related Party in a country:

(i) following Regulatory Approval of such Licensed Product in that country, if a Regulatory Approval or similar marketing approval is required in such country; or

(ii) at any time, if no such Regulatory Approval or similar marketing approval is required in such country;

(nn) "**FSA**" means the feasibility study agreement dated 18 October 2019 pursuant to which the Client and OXB commenced preliminary activities for the eventual supply by OXB of cGMP lentiviral vectors targeting the Client's gene(s) of interest;

(oo) "**FTE**" means a full-time equivalent person year (consisting of 1568 hours per year);

(pp) "**GAAP**" means generally accepted accounting principles in the U.S. consistently applied;

(qq) "**GBP**" and "**£**" mean the lawful currency of the United Kingdom;

(rr) "**GOI**" means [***];

(ss) "**ICH**" means International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use;

(tt) "**IM Date**" means the date upon which Manufacture of a Batch is initiated;

(uu) "**Initial Fee**" means the upfront fee pursuant to clause 7.1 and set out in Schedule 2;

(vv) "**Initial Target**" means [***];

(ww) "**Insolvency Event**" in relation to a Party or entity shall mean any of the following events: (i) that Party ceasing or threatening to cease to carry on business; (ii) that Party being deemed by a competent authority to be unable or admitting inability to pay its debts; (iii) a moratorium is declared by a competent authority in respect of any indebtedness of that Party; (iv) that Party giving notice to any of its creditors that it has suspended or is about to suspend payment of any of its debts; (v) that Party commencing negotiations with one or more of its creditors with a view to rescheduling any of its indebtedness by reason of financial difficulties; (vi) an arrangement, composition, or assignment with or for the benefit of its creditors is entered into or proposed by or in relation to that Party; (vii) a receiver, administrative receiver, liquidator, or compulsory manager taking possession of or being appointed over the whole or any material part of the assets of that Party; (viii) any expropriation, attachment, sequestration, distress, execution or other analogous process is levied or enforced on or affects the whole or any material part of the assets of that Party (and is not discharged within [***]); (ix) enforcement of any mortgage, charge, pledge, lien or other security interest securing any obligation of any person or any other agreement or arrangement having a similar effect over any assets of that Party; (x) that Party or its directors or the holder of a qualifying floating charge giving notice of his, their or its intention to appoint an administrator; (xi) that Party or its directors or any of its creditors or the holder of a qualifying floating charge making an application to the court for the appointment of an administrator; (xii) an administrator being appointed of that Party; (xiii) the winding-up, dissolution, administration or reorganisation (by way of voluntary arrangement, scheme of arrangement or otherwise) with respect to that Party; provided that this does not apply to any winding-up petition that is frivolous or vexatious and is discharged, stayed or dismissed within [***] of commencement; (xiv) that Party being struck off the register of companies; or (xv) the happening in relation to that Party of an event analogous to any of the above in any jurisdiction in which it is incorporated or resident or in which it carries on business or has assets;

(xx) "**Intellectual Property Rights**" means all rights in Patent Rights; rights to inventions, copyright and related rights; rights in trade marks, trade names and domain names; rights in designs; rights in computer software; database rights; rights in confidential information (including know-how) and any other intellectual property rights; in each case whether registered or unregistered and including all applications (or rights to apply) for, and renewals or extensions (for

their full term) of, such rights and all similar or equivalent rights or forms of protection which subsist or will subsist now or in the future in any part of the world;

(yy) "**Know-How**" means unpatented information that is not in the public domain (including, without limitation, information comprising or relating to inventions, discoveries, concepts, methodologies, models, research, development and testing procedures, the results of experiments, tests and trials, manufacturing processes, techniques and specifications, quality control data, analyses, reports and submissions);

(zz) An individual shall be deemed to have "**Knowledge**" of a particular fact or other matter if (i) such individual is actually aware of such fact or other matter, or (ii) a prudent individual could reasonably be expected to have discovered or otherwise become aware of such fact or other matter under the circumstances by virtue of conducting a reasonable investigation or otherwise;

(aaa) "**Licensed Product**" means [***];

(bbb) "**Manufacture**", "**Manufactured**" and "**Manufacturing**" means the steps, Processes and activities to produce any Vector for clinical supply, including the manufacturing, processing, handling, storage, packaging, labelling, validation, testing, release and preparation for Delivery of Vector;

(ccc) "**Manufacturing Slot**" means a scheduled period during which OXB will Manufacture a Batch at a Facility as specified in the applicable Scope of Work or Work Order or Change Order;

(ddd) "**Manufacturing Slot Deposit**" shall have the meaning set out in Schedule 1;

(eee) "**Manufacturing Slot Deposit Payment Date**" means, in respect of each Manufacturing Slot, the date that is [***] before the applicable scheduled IM Date for the Manufacturing Slot;

(fff) "**Master Production Batch Record**" means the technical documents that define the Manufacturing procedures and associated materials for a specific part of the Manufacturing process, as approved by both Parties and as amended by the Parties in writing from time to time;

(ggg) "**Milestone Payment**" means one of the milestone payments set out in Schedule 2;

(hhh) "**Net Sales**" means the gross amount invoiced by a Related Party(ies) in arms-length transactions for or on account of the sale to a non-Related Party of Licensed Products, less the sum of the following:

(i) [***];

(ii) [***];

(iii) [***];

(iv) [***]; and

(v) [***].

[***].

[***].

[***]:

(i) [***]; or

(ii) [***],

[***].

It is understood that any accruals for individual items reflected in Net Sales are periodically (at least once each calendar quarter) trued up and adjusted by each Related Party consistent with its customary practices and in accordance with GAAP.

Sale or transfer of Licensed Products between any of the Related Parties shall not result in any Net Sales, with Net Sales to be based only on any subsequent sales or dispositions to a non-Related Party;

(iii) "**OXB Arising IPR**" shall have the meaning attributed to it in clause 12.5;

(jjj) "**OXB IP**" means:

(i) the Patent Rights that Cover the manufacture or use of Vectors, or the manufacture, use, research, Development or Commercialisation of the Licensed Products, including those Patents identified in Schedule 5 (the "**Licensed Patents**"); and

(ii) the Know-How that is necessary or reasonably useful for the manufacture or use of Vectors, or the manufacture, use, research, Development or Commercialisation of Licensed Products (the "**Licensed Know-How**");

in each case, to the extent Controlled by OXB as of the Effective Date or during the Term, including Intellectual Property Rights subsisting in its Background IPR and the OXB Arising IPRs;

(kkk) "**OXB Manufacturing Process**" means the Manufacturing process used by OXB to manufacture a Vector or which is made available by OXB to Client or Client's Affiliate or a Third Party pursuant to any Technology Transfer;

(lll) "**OXB Patent Rights**" means Patent Rights Controlled by OXB;

(mmm) "**Parties**" means OXB and Client and "**Party**" shall mean either of them;

(nnn) "**Pass-Through Costs**" means any documented external costs that are (a) agreed in a Work Order or otherwise in writing by Client and incurred by OXB in carrying out the Manufacturing and Services, including Technology Transfer, under this Agreement or (b) identified in the relevant Work Orders (including where the Work Order contains an estimate for such costs, the final costs incurred by OXB) and will include without limitation the costs of Plasmids for both research and the Manufacture of cGMP grade Vector, and in each case shall not include those costs included in the Batch Fee;

(ooo) "**Patent Rights**" shall mean all patents (including all reissues, extensions, substitutions, confirmations, re-registrations, re-examinations, invalidations, supplementary protection certificates and patents of addition) and patent applications (including all provisional applications, continuations, continuations-in-part and divisionals), and foreign equivalents of any of the foregoing;

(ppp) "**Phase I Clinical Trial**" means a human clinical trial normally conducted in healthy volunteers or diseased patients with the aim of determining the pharmacokinetics, pharmacodynamics, early safety profile and some preliminary evidence of efficacy if conducted in patients;

(qqq) "**Phase 2/3 Clinical Trial**" means a human clinical trial involving a sufficient number of subjects that, prior to commencement of the trial or at any other defined point in the trial, satisfies both of the following ((i) and (ii)):

(i) such trial is designed to (1) establish that the Licensed Product is safe and efficacious for its intended use, and (2) define and determine warnings, precautions, and adverse reactions that are associated with the Licensed Product in the dosage range to be prescribed, which trial is intended to support Regulatory Approval in any country; and

(ii) such trial is or becomes a registration trial sufficient for filing an application for Regulatory Approval in any country, as evidenced by (1) an agreement with or statement from the relevant Regulatory Approval on a special protocol assessment or equivalent, or (2) other guidance or minutes issued by the relevant Regulatory Approval, for such registration trial;

(rrr) "**Pivotal Clinical Trial**" means a pivotal human clinical trial conducted in a sufficient number of patients to establish safety or efficacy in the particular indication tested, the data and results of which are intended to be used as part of a basis for seeking Regulatory Approval in any country;

(sss) "**Plasmids**" means the plasmids required to Manufacture Vector, including genome and packaging components, as specified in the applicable Scope of Work or Work Order or Change Order;

(ttt) "**Process**" means the processes and procedures used to Manufacture Vector in accordance with the Master Production Batch Record, including all protocols and SOPs referenced therein. Process will not include Facility design and SOPs generated or used in the course of performing services that are generally applicable to OXB's business, such as in connection with the operation of any of its Facility and/or equipment, and that a reasonable contract manufacturing organisation skilled in the art would be expected to have in place for the operation of its own facility;

(uuu) "**Project Manager**" shall have the meaning set out in clause 2.1;

(vvv) "**Quality Agreement**" shall have the meaning set out in clause 3.3(a);

(www) "**Regulatory Approval**" means all technical, medical, and scientific licenses, registrations, authorisations, consents, and approvals of any Regulatory Authority, necessary for the use, development, manufacture, and

commercialisation of a Vector or Licensed Product in a given regulatory jurisdiction;

(xxx) "**Regulatory Authority**" means any national, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity with authority over the manufacture, production, use or storage or transport, of any Vector or Licensed Product, including the FDA, the EMA, and the European Commission (and any successor agencies), in (i) the United States of America, (ii) the United Kingdom, (iii) the European Union, and (iv) such other territories as may be mutually agreed to by the Parties in writing;

(yyy) "**Regulatory Milestones**" shall have the meaning given to it in Schedule 2;

(zzz) "**Regulatory Milestone Payments**" shall have the meaning given to it in Schedule 2;

(aaaa) "**Related Party**" shall mean Client and its sublicensees of one or more Licensed Products. For clarity, Related Party shall not include any distributors, wholesalers or the like unless such entity is an Affiliate of Client;

(bbbb) "**Representatives**" shall have the meaning set out in clause 14.2;

(cccc) "**Royalties**" shall have the meaning set out in clause 7.12;

(dddd) "**Royalty Term**" means, on a Licensed Product-by-Licensed Product and country-by-country basis, the period commencing on the First Commercial Sale of such Licensed Product in such country and ending the later of (i) the [***] of the First Commercial Sale of the given Licensed Product in such country and (ii) to the extent there is a Valid Claim within the OXB IP that Covers (A) the manufacture of the Vector used to generate such Licensed Product or the manufacture of the Licensed Product or (B) the sale of the Licensed Product, in each case (A) or (B) in such country, the expiration of the last such Valid Claim. A true and complete list of Patent Rights within the foregoing sub-clause (ii) is provided in Schedule 5, which Schedule 5 may be updated by OXB, on a Vector-by-Vector basis, in the event of any change to the status of the relevant Patent Rights;

(eeee) "**Sample**" means any sample of Vector for analytics, retention, stability studies or other non-clinical purpose;

(ffff) "**Scope of Work**" means a document signed by both Parties setting out the agreed Services for each Target to be provided by OXB to Client under this Agreement which shall include a description, the duration, and the cost of the Services and individual Work Package(s). Agreed Scopes of Work shall be incorporated into and form part of this Agreement and may be modified from time to time by a Change Order or a Work Order;

(gggg) "**Senior Officers**" means (i) for OXB, the CEO or duly authorized designee and (ii) for Client, the CEO, CFO or duly authorized designee;

(hhhh) "**Service Fee**" shall mean the fees and other payments and costs for the Services other than Batch Manufacturing Services (which shall be charged in accordance with the Batch Fee);

(iiii) "**Services**" shall mean any Manufacturing services and/or other services to be performed by OXB under this Agreement, as described in any Scope of Work, Work Package or Work Order or Change Order;

(jjjj) "**SOPs**" means the written standard operating procedures and methods of OXB, as the same may be amended, in OXB's sole discretion, from time to time; provided that any change to the SOPs that could impact Client's ability to Develop or Commercialise the Licensed Product shall be subject to clause 3.4;

(kkkk) "**Specification**" means with respect to each Vector, the tests, references to analytical methods and appropriate acceptance criteria (including yield) and attributes to which such Vector must conform, as set forth in the Quality Agreement or agreed from time to time in writing by Client and OXB pursuant to clause 3.4;

(llll) "**Specification Changes**" shall have the meaning attributed to it in clause 3.4;

(mmmm) "**Storage Guidelines**" means those procedures, methods and conditions for preserving, monitoring and storing all Client Materials, Components, and Batches of Vector, as set forth in the Quality Agreement or as otherwise mutually agreed to in writing by the Parties;

(nnnn) "**Supply Term**" shall have the meaning set out in clause 17.1(a);

(oooo) "**Target**" or "**Targets**" means the Initial Target and any Additional Targets deemed to be a "Target" herein or any of them individually, as applicable;

(pppp) "**Technology Transfer**" means the technology transfer process described in Article 13 occurring after a Technology Transfer Event, under which process OXB provides documentation, technical assistance, materials and cooperation by appropriate employees (including technical training at an OXB site pertaining to the Process) as set forth in the Technology Transfer Plan and as is reasonably necessary for properly skilled personnel of Client or its Affiliate or its Third-Party designee (as applicable) to Manufacture a Vector in accordance with the applicable Process;

(qqqq) "**Technology Transfer Event**" has the meaning set out in Schedule 3;

(rrrr) "**Technology Transfer Milestone**" shall have the meaning set out in Schedule 2;

(ssss) "**Technology Transfer Milestone Payments**" shall have the meaning set out in Schedule 2;

(tttt) "**Term**" shall have the meaning set out in clause 17.1;

(uuuu) "**Testing Laboratory**" means a qualified independent Third-Party testing laboratory reasonably acceptable to both Parties by written agreement to evaluate certain technical issues and/or detect their root causes;

(vvvv) "**Third Party Cell Line**" shall have the meaning set out in clause 3.10;

(wwww) "**Third Party**" means any person or entity other than Client, OXB and their respective Affiliates;

(xxxx) "**USD**" or "**US$**" means the lawful currency of the United States;

(yyyy) "**Valid Claim**" means a claim of (i) an unexpired and issued patent that has not been disclaimed, revoked, or held invalid, un-patentable or unenforceable by an administrative agency, court or other government agency of competent jurisdiction in a final and non-appealable decision (or a decision un-appealed within the time limit allowed for appeal), and which has not been admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise; or (ii) a pending patent application that has not been finally rejected by a patent office or other governmental agency of competent jurisdiction in an un-appealable decision or a decision that is un-appealed within the time allowed for appeal and that has been prosecuted in good faith and has not been pending for more than [***] from the date of its earliest priority date;

(zzzz) "**Vector**" means a lentiviral vector delivering the applicable GOI that is (i) Manufactured and supplied under this Agreement by OXB or an Approved Subcontractor of OXB; (ii) Manufactured by Client following a Technology Transfer to Client pursuant to Article 13 with respect to such vector delivering the applicable GOI; or (iii) Manufactured by Client's Affiliate or a Third Party on behalf of Client or its sublicensee following a Technology Transfer to such Affiliate or Third Party pursuant to Article 13 with respect to such vector delivering the applicable GOI;

(aaaaa) "**Work Order**" means a document signed by both Parties setting out new Work Packages to be added to a Scope of Work;

(bbbbb) "**Work Package**" means the work identified as a discrete work package in a Scope of Work, Change Order or Work Order thereto; and

(ccccc) "**Year**" means a calendar year starting on 1 January and ending on 31 December.

1.2 **Interpretation**. In this Agreement:

(a) unless otherwise specified, references to clauses and schedules are to the clauses and schedules of this Agreement**;**

(b) the words "include", "including" and "in particular" are to be construed as being by way of illustration or emphasis only and are not to be construed so as to limit the generality of any words preceding them;

(c) the words "other" and "otherwise" are not to be construed as being limited by any words preceding them;

(d) headings are used for convenience only and do not affect its interpretation; and

(e) a reference to the singular includes a reference to the plural and vice versa and a reference to any gender includes a reference to all other genders.

1.3 **Termination of CDA and FSA**.

(a) The Parties agree that the CDA is hereby terminated in all respects and with effect from the date of this Agreement the CDA shall have no further effect except to the extent that certain provisions of the CDA survive any expiration or termination pursuant to the terms of the CDA**.**

(b) The Parties agree that the FSA is hereby terminated in all respects and with effect from the date of this Agreement the FSA shall have no further effect except to the extent that (i) certain provisions of the FSA survive any expiration or termination pursuant to the terms of the FSA or (ii) activities due to be carried out under the FSA are incomplete in which case such activities shall continue under this Agreement.

(c) In the event of any conflict between the terms and provisions of the CDA or FSA and the terms and provisions of this Agreement, including with respect to the use and treatment of Confidential Information, this Agreement will prevail.

2. Governance

2.1 **Representatives**. Within [***] of the Effective Date, each of OXB and Client shall appoint an employee as a project manager to oversee their respective obligations under this Agreement (each a "**Project Manager**"). Unless agreed otherwise between the Parties in writing, all communications between OXB and Client regarding the conduct of OXB's day-to-day performance will be with the respective Party's Project Manager. A Party may change its Project Manager at any time by providing at least [***] prior written notice to the other Party. Client shall incur no cost for any change in OXB's Project Manager, including, without limitation, costs associated with any knowledge transfer to a new OXB Project Manager.

2.2 **Steering Committee**

(a) **Steering Committee**. Within [***] after the Effective Date, the Parties shall establish a steering committee (the "**Steering Committee**") by each Party designating and notifying the other Party of its initial members to serve on the Steering Committee. The Steering Committee will remain in place until the termination or expiry of the Term and, unless otherwise agreed in writing between the Parties, will be disbanded at the end of such period.

(b) **Role of Steering Committee**. The Steering Committee shall lead and oversee the performance of OXB under this Agreement and, subject to clause 2.2(g), shall be responsible for and have authority for:

(i) providing a forum for strategic decision-making;

(ii) reviewing performance under this Agreement;

(iii) resolving any disputes referred to it by the Project Team; and

(iv) making such other determinations as are expressly delegated to it under the terms of this Agreement.

(c) **Membership**. The Steering Committee shall consist of two senior personnel of OXB and two senior personnel of Client, in each case with authority to make decisions for the appointing Party on issues within the mandate of the Steering Committee and shall additionally include each Party's Project Manager. Each member shall have the appropriate background and expertise to contribute to the Steering Committee. Each Party may change its members on the Steering Committee from time to time by providing notice in writing to the other Party. Either Party may, from time to time, invite additional representatives or consultants, who are not Steering Committee members but who have knowledge and/or experience in relation to the performance of the collaboration

between the Parties, to attend Steering Committee meetings. Prior to attendance of any Steering Committee meeting, all of the Steering Committee members and all other permitted attendees must be bound by confidentiality obligations at least as protective to the other Party's Confidential Information as the terms set out in Article 14.

(d) **Co-Chairpersons**. Each Party shall appoint one of its members to co-chair Steering Committee meetings (each a "**Co-Chairperson**"). The Co-Chairpersons shall attend meetings, ensure the orderly conduct of meetings, and ensure that written minutes of each meeting are taken and issued to each of the Parties.

(e) **Meetings**. The Steering Committee shall meet as often as agreed by the Co-Chairpersons, but in no event less than [***]. Such meetings may be conducted by telephone, videoconference or in person as determined by the Co-Chairpersons, acting reasonably. Each Party may also call for special meetings of the Steering Committee with reasonable prior notice (it being agreed that at least [***] shall constitute reasonable notice), to resolve particular matters within the decision-making responsibility of the Steering Committee. Meetings of the Steering Committee shall be effective only if at least one (1) representative of each Party is present and participating as a Co-Chairperson.

(f) **Decision-Making**. The Steering Committee will endeavour to make decisions by consensus of the Co-Chairpersons with each Party having one (1) vote. If a dispute or failure to agree arises which cannot be resolved within the Steering Committee, the Steering Committee shall cause such dispute or failure to agree to be referred to the Senior Officers (or their respective delegates) for resolution. The Senior Officers (or their respective delegates) shall attempt in good faith to resolve such dispute or failure to agree. In the event that the Senior Officers (or their respective delegates) have been unable to resolve such dispute within [***] of the dispute being referred to them, either Party may seek resolution of the dispute in accordance with clause 18.14.

(g) **Limits**. Each of the Steering Committee, the Project Team and the Project Managers shall only have the powers assigned expressly to each of them in this Agreement. Notwithstanding any provision to the contrary, neither the Steering Committee nor the Project Team nor the Project Managers shall have any power to amend or modify the provisions of, or to waive compliance with, this Agreement (including any Scopes of Work, Work Packages or Work Orders), and each Party shall retain the rights, powers and discretion granted to it under this Agreement and no such rights, powers or discretion shall be delegated to or vested in the Steering Committee, the Project Team or the Project Managers. For clarity and without limiting the foregoing, neither the Steering Committee nor the Project Team nor the Project Managers shall have any power to agree to any Specification Changes, which are subject to the process set forth in clause 3.4.

2.3 **Project Team**

(a) Within [***] after the Effective Date, the Parties will establish a project team ("**Project Team**") which shall consist of each Party's Project Manager and such other employees, or, subject to the approval of the other Party, which shall not be unreasonably withheld or delayed, representatives or consultants of a Party as considered necessary to attend by such Party's Project Manager. Prior to attendance of any Project Team meeting all such employees, representatives

and consultants of a Party must be bound by confidentiality obligations at least as protective to the other Party's Confidential Information as the terms set out in Article 14. The Project Team shall:

(i) provide a forum for, and facilitate, communications between the Parties with respect to the provision of Services by OXB;

(ii) have operational responsibility for co-ordinating the performance of the Scopes of Work and Work Packages;

(iii) have responsibility for proposing an amendment or termination of existing Scopes of Work or Work Packages, and establishing new Scopes of Work or Work Packages; provided however that any new or amended Scopes of Work or Work Packages or any termination of a Scopes of Work or Work Package must be mutually agreed to in a written document executed by an authorised representative of each Party in order to become effective; and

(iv) subject to clause 2.3(c), shall be responsible for promptly referring any dispute not resolved within [***] to the Steering Committee for resolution.

(b) The Project Team shall hold meetings as often as the Project Managers agree is necessary during the Term. Project Team meetings may be held face to face, or by tele- or video-conference, at such times and places as are agreed to by the Parties acting reasonably. All decisions of the Project Team will be made by consensus of the Project Managers, and any failure to agree will be referred to the Steering Committee for resolution.

(c) At Client's reasonable request, time sensitive disputes will be eligible for an accelerated dispute review process under which (i) any dispute not resolved by the Project Team within [***] will be referred to the Steering Committee and (ii) any dispute not resolved by the Steering Committee within [***] after referral to the Steering Committee will be escalated in accordance with clause 2.2(f).

2.4 **Additional Targets**. At any time during the Term, Client may request by written notice to OXB that one or more Additional Targets be included within the scope of this Agreement. Each Additional Target requested by Client and consented to in writing by OXB shall, subject to payment by Client to OXB of the Additional Target Fee in accordance with clause 7.2, be deemed a Target under this Agreement. The Parties shall agree and sign a Scope of Work setting out the Services in relation to each Additional Target, which once signed by both Parties shall be incorporated into and be part of this Agreement.

3. Provision of Services

3.1 **Provision of Services**. The Services will be provided by OXB in accordance with the applicable Scope of Work. In the event the Client wishes to amend the Scope of Work, Client will request the work it wishes OXB to perform identifying the Work Packages to be amended, added or terminated. OXB will promptly provide Client with a draft Change Order or Work Order as applicable for review by Client, and once the Parties have agreed the draft Change Order or Work Order, OXB will issue a final version for signature by both Parties. Once a Change Order or Work Order has been signed by both Parties the Scope of Work shall be deemed amended in accordance with such Change Order or Work Order. All signed Change Orders and Work Orders shall be

subject to the terms and conditions of this Agreement. In the event of any conflict between the terms and provisions of any Scope of Work, Change Order or Work Order and the terms and provisions of this Agreement, this Agreement will prevail unless the relevant term of this Agreement is expressly varied by the written agreement of the Parties set forth in the applicable Scope of Work, Change Order or Work Order.

3.2 **General Standards**

(a) OXB shall perform the Services in accordance with the terms and conditions of this Agreement and Applicable Law, and in a professional and workmanlike manner, and in accordance with the activities, timeline and budget set forth in the applicable Scope of Work, Work Order or Change Order.

(b) Upon Delivery, OXB shall ensure Batches have been Manufactured in accordance with Applicable Law, including cGMP, the Process, the Specifications and the Quality Agreement.

(c) In the course of performing its obligations under this Agreement, OXB and its Affiliates shall not employ or use the services of any person that has been debarred, for example as under Subsection (a) or (b) of Section 306 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 335a) or any comparable provision of any other Applicable Laws. OXB shall notify Client immediately in the event that OXB becomes aware of such debarment or threatened debarment of any of its employees (or any other person) engaged in the provision of Services under this Agreement.

(d) Without limiting OXB's obligation to comply with Applicable Law, OXB will comply with the UK Anti-Bribery Law and the OECD Anti-Bribery Convention with regard to Services and Manufacturing, including not offering or giving anything of value to a foreign public official in connection with the performance of the official's duties or inducing an official to use their position to influence any acts or decisions of any foreign, state or public international organization, and other similar laws and regulations, as well as all applicable export control and economic sanctions laws and regulations.

(e) OXB will ensure that documents provided to Client in connection with this Agreement are provided in English.

3.3 **Quality Agreement; [***]**.

(a) Prior to Manufacture of the first Batch, the Parties will negotiate and enter into a detailed document allocating the technical quality responsibilities of the Parties with respect to the Manufacture and Delivery of Batches (such executed document, a "**Quality Agreement**"), which will be attached hereto as Schedule 7 upon completion. In the event of any conflict between the terms and provisions of this Agreement and the terms and provisions of the Quality Agreement, with respect to quality-related activities, including compliance with cGMP, the provisions of the Quality Agreement will prevail, and with respect to all other activities or issues this Agreement will prevail.

(b) [***].

3.4 **Changes to Specifications**. In each case subject to clause 3.11:

(a) Amendments, modifications and additions to the Specifications ("**Specification Changes**"), the Manufacturing Process of a Batch ("**Process Changes**"), or the quality of Components ("**Component Changes**") may only be made upon mutual written agreement between the Parties in each case, in accordance with the applicable provisions of the applicable Quality Agreement. If Specification Changes, Process Changes or Component Changes are so agreed to by the Parties, OXB shall promptly implement the same. The cost allocation between the Parties for any other Specification Changes, Process Changes and Component Changes will be as agreed to by the Parties in writing.

(b) Notwithstanding clause 3.4(a), OXB shall use commercially reasonable efforts to implement any reasonable Specification Changes, Process Changes or Component Changes which are requested by Client (each, a "**Requested Change**"), provided that:

(i) such Requested Change does not affect the cost to OXB of performing the relevant Services (unless Client agrees in writing to cover such costs), or require Client to perform Services materially different from those described in the applicable Scope of Work, Work Order or Change Order, or require OXB to breach any contractual obligations owed to, or to incur any additional expense in relation to (unless Client agrees in writing to cover such costs) in relation to any other customer; and

(ii) if OXB notifies Client of a reasoned technical concern regarding such Requested Change and if Client nevertheless wishes to evaluate the potential implementation of the Requested Change, then: (1) the Parties will enter into a Scope of Work or Work Order for one or more pilot batch(es) implementing the Requested Change; (2) if Client deems the pilot batch(es) successful, the Parties will work together in good faith to align on implementation of the Requested Changes, taking into account the results of the pilot batch(es); and (3) if the Parties are able to come to such agreement, the Parties shall execute a Change Order in accordance with clause 3.1 and OXB will promptly implement the applicable changes, in accordance with the Change Order.

(c) To the extent necessary, the Parties shall amend the Quality Agreement and Scope of Work or Work Order to reflect any such Specifications Changes, Process Changes and Component Changes agreed in writing by the Parties. Without limiting the foregoing, for clarity, no Specification Changes, Process Changes or Component Changes will be implemented by OXB without the prior written consent of Client in each instance.

3.5 **Facility**. OXB shall Manufacture the Batches exclusively at the Facilities. OXB shall not change the location of the Facility, or use any additional facility, for the performance of cGMP Manufacture under this Agreement without at least [***] prior written notice to, and prior written consent from, Client, which consent will not be unreasonably withheld or delayed (it being understood and agreed that Client may withhold consent pending satisfactory completion of a quality assurance audit and/or regulatory impact assessment of the new location or additional facility, as the case may be). OXB shall bear OXB's costs of, as well as any actual and reasonable out- of-pocket costs incurred by Client in connection with, any change in Facility that is not requested by Client. OXB will maintain, at its own expense, OXB's Facility and all equipment required for the Manufacture of Vector by OXB in a state of repair and operating efficiency consistent with the requirements of all Applicable Law, including cGMP if applicable.

3.6 **Subcontracting**. OXB shall be entitled to subcontract its obligations under this Agreement, in whole or in part, to the subcontractors approved by Client in advance as specified in the Quality Agreement (or, with respect to non-cGMP Services, to the approved subcontractors as set out in the applicable Scope of Work) (such subcontractors collectively, the "**Approved Subcontractors**"). OXB shall ensure that all Approved Subcontractors are bound by obligations to perform which are consistent with the terms of this Agreement, including, as applicable, confidentiality, quality assurance and regulatory obligations. OXB shall remain responsible for the performance of any subcontracted responsibilities and shall be liable for the acts and omissions of all of its subcontractor(s) in connection with performance under this Agreement as if such acts or omissions were performed by OXB; provided always that, for the avoidance of doubt, OXB shall not have any greater liability to Client than it would have under this Agreement than if OXB had carried out such work and/or committed such breach causing the liability itself.

3.7 **Procurement**. OXB shall, at its cost, purchase, qualify, test, inspect and approve all Components and shall ensure that the Components are of suitable quality as required under the Specifications.

3.8 **Plasmids**.

Unless otherwise agreed in writing by the Parties, Client will notify OXB in writing which of the following will apply to the Manufacture of a Vector:

(a) Plasmids incorporating a GOI (genome/transfer Plasmid) suitable for Manufacturing Vector shall be procured and provided to OXB by Client at Client's sole cost;

(b) Plasmids incorporating a GOI (genome/transfer Plasmid) shall be procured by OXB on behalf of Client from an Approved Subcontractor and will be deemed Client Materials after Client's payment therefor. [***]Pass-Through Costs relating to the manufacture of such Plasmids shall be charged by OXB to Client, such costs to include the direct cost of Plasmids, their transport and storage, and any import duties. In addition to such Pass-Through Costs, Client shall pay OXB a handling fee for procuring such Plasmids, which shall be [***] of such external costs and shall cover all OXB's internal and other external costs associated with procuring such Plasmids (including stability testing performed by OXB). In such circumstances, OXB will notify Client in writing of the total costs for such Plasmids in advance of them being incurred. OXB will invoice Client following receipt by OXB of an applicable invoice from the Plasmid manufacturer. Title to such Plasmids shall pass to Client upon Client's payment to OXB of the Pass-Through Costs (including the handling fee) for such Plasmids, and OXB shall inspect, store and handle such Plasmids in accordance with the provisions of this Agreement governing Client Materials. Notwithstanding any other provision of this Agreement, OXB accepts no liability for the performance of the Plasmid manufacturer under this sub-clause 3.8(b) however the Plasmids are sourced and in particular, in the event the Plasmid manufacturer fails to perform or delivers defective Plasmids to OXB, other than to the extent resulting from OXB's gross negligence or wilful misconduct; or

(c) Helper Plasmids, i.e. env, rev and gag-pol Plasmids, shall be procured by OXB from an Approved Subcontractor at OXB's sole cost and will be deemed Components.

3.9 **Sequences**. If applicable to the Services being performed, Client will inform OXB of the sequence of any nucleic acid construct it supplies to OXB (such as the GOI, plasmids, vectors, etc.) and will allow OXB to perform sequencing of such construct (either in-house or using an Approved Subcontractor) to enable OXB to comply with safety requirements and to ensure nucleic acid constructs are sufficiently characterised to support project progression. For clarity, all such information, shall be deemed Confidential Information of Client; provided however that Client acknowledges and agrees that it may be necessary for OXB to share certain Confidential Information of Client, including the sequence of any nucleic acid in the Plasmids, with the manufacturer of such Plasmids including for export clearance purposes. In each case provided that the extent of Client's Confidential Information shared by OXB with a Plasmid manufacturer is limited to the Confidential Information that such Plasmid manufacturer reasonably needs to know for the purposes of manufacturing and providing such Plasmids to OXB for use in performing the Services under this Agreement: (a) Client accepts all risk relating to the provision of such Confidential Information by OXB to the correct Plasmid manufacturers, (b) such Plasmid manufacturers shall not be deemed to be Representatives of OXB for the purposes of clauses 14.2 and 14.3 and (c) OXB shall have no liability for any acts or omissions of such Plasmid manufacturers to the extent that Confidential Information of Client is disclosed pursuant to this clause.

3.10 **Cell Lines**. In the event Client requests or a Scope of Work or Work Order requires that OXB use a cell line for which OXB does not have a use right or licence (each, a "**Third Party Cell Line**"), OXB shall request the proposed licence terms from the relevant Third Party, and upon receipt of such licence terms shall provide them to Client for consideration. If Client provides written approval of the licence terms, OXB shall seek in good faith to procure the licence to use such Third Party Cell Line in the provision of Services on such licence terms, and Client shall reimburse the consideration paid by OXB to the Third Party for such licence (in accordance with the licence terms as approved by Client) and OXB's actual, reasonable and documented costs in relation to obtaining such a licence. For the avoidance of doubt, OXB shall not and shall not be required to use any such Third Party Cell Line in the provision of Services unless and until Client has given its written approval for OXB to obtain, and OXB has obtained, a licence to use such Third Party Cell Line in the provision of Services in accordance with this clause 3.10.

3.11 **Good Manufacturing Practice**. Each Party shall promptly notify the other Party upon becoming aware of any material amendments of, or additions to, cGMP that could affect the Services to be performed by OXB under this Agreement and applicable Scope of Work or Work Order. The Parties shall confer with each other about the best means of complying with such amendments or additions. Changes to the Scope of Work or Work Order resulting from changes to cGMP may be proposed by either Party in writing to the other Party, but shall take effect only subject to the signature by both Parties of an appropriate Change Order; provided that OXB shall use commercially reasonable efforts to implement any reasonable change to the Services required as a result of any amendment or addition to cGMP ("**Required cGMP Change**"). OXB shall bear the cost of any Required cGMP Change if such change applies to the services OXB provides to other clients or otherwise applies to OXB's business as a contract manufacturing organization generally. Any other Required cGMP Changes shall be for the sole cost of Client, unless otherwise agreed under the applicable Change Order. Notwithstanding the foregoing, OXB shall not be required to act in any way in contravention of any newly implemented legal or other regulatory requirements.

3.12 **Permits and Approvals**. OXB shall obtain and maintain all government permits and government licences, including health, safety and environmental permits, necessary

for the conduct of the Services as required by Applicable Law. Without prejudice to any of Client's other rights under this Agreement or the Quality Agreement, OXB shall inform Client promptly (within [***]) in writing in the event any license, permit, or approval required by any Regulatory Authority for the Manufacture and supply of Vector by OXB is not obtained in a timely manner or is withdrawn or is otherwise under investigation.

4. Client Materials

4.1 **Client Materials**. Client will provide OXB with sufficient quantities of Client Materials to enable OXB to perform the Services as set out in the Scope of Work and applicable Work Orders. Client will ensure that all related documents provided to OXB are in English.

4.2 **Delivery and Title**.

(a) Client Materials provided by Client shall be delivered free of charge DDP (INCOTERMS 2020) OXB's Facility.

(b) Client will retain title to and ownership of Client Materials at all times. OXB shall not impose or cause to be imposed any claims, encumbrances and liens on Client Materials. OXB will at all times label or otherwise designate the Client Materials as property of Client. Client Materials will remain in the possession, control and care of OXB following delivery of such Client Materials to OXB. OXB will not transfer the Client Materials to any Third Party except to Approved Subcontractors without Client's consent, and will use, store and handle the Client Materials in accordance with the Storage Guidelines and (a) solely on behalf of Client, (b) with due care and, where applicable, in compliance with cGMP, any specifications provided by Client and in accordance with the Scope of Work or Work Order or Change Order, and (c) solely for the purposes of providing Services pursuant to this Agreement. OXB shall not (or allow any Third Party to) use the Client Materials for any other purpose, and without limiting the generality of the foregoing, will not analyse, characterize, modify or reverse engineer any Client Materials or take any action to determine the structure or composition of any Client Materials unless required to perform the Services pursuant to a signed Work Order. OXB shall destroy or return to Client all unused quantities of Client Materials according to Client's written directions and at Client's sole cost and expense. Title to the Client Materials will at all times remain with Client. While in the possession, control or care of OXB, OXB will have the risk of destruction, theft or loss of Client Material, except that OXB will only bear the risk of destruction or loss occurring during the manufacturing, processing, validation, testing or release of Vector to the extent caused by OXB's failure to comply with Applicable Law or the negligence or the wilful misconduct of OXB.

4.3 **Material Safety Data Sheets**. Client will provide OXB with accurate and complete material safety data sheets for all Client Materials and other relevant and necessary information concerning the safety, handling, use, disposal and environmental effects of such Client Materials.

4.4 **Import and Export**. Client will be responsible at its sole cost and expense for satisfying all import, export and customs requirements in relation to Client Materials, including U.S. export control regulations. Client or its Third-Party designee will be the importer and exporter of record for any materials being imported and shipped to OXB and for all materials exported from the United Kingdom.

5. Forecasting and Ordering for Batches

5.1 Upon execution of this Agreement by the Parties and subject to the payment schedule in Scope of Work for #CP0188 entered into by the Parties on or about the Effective Date (the "**Initial Scope of Work**"), Client shall pay to OXB the Manufacturing Slot Deposit for all Manufacturing Slots identified in the Initial Scope of Work. Thereafter, following execution by the Parties of any new Scope of Work or Work Order, OXB will invoice Client for the Manufacturing Slot Deposits for each Manufacturing Slot set out in such new Scope of Work or Work Order, and Client will pay each Manufacturing Slot Deposit on or before the applicable Manufacturing Slot Deposit Payment Date.

5.2 In the event Client wishes to procure additional Manufacturing Slots it will inform OXB and, pursuant to clause 3.1, OXB will provide a draft Scope of Work or Work Order setting out the anticipated IM Date and the applicable Batch Fee. Upon signature of an agreed Scope of Work or Work Order, OXB shall invoice Client for the applicable deposit for each Manufacturing Slot set out in the Scope of Work or Work Order, and Client will pay such Manufacturing Slot Deposit on or before the Manufacturing Slot Deposit Payment Date.

5.3 If there is a change to project timelines requested by Client which affects any binding Manufacturing Slots, Client and OXB will discuss in good faith re-scheduling of such Manufacturing Slots and if the Parties agree to reschedule a Manufacturing Slot, OXB will issue a Change Order setting out the rescheduled Manufacturing Slots, and if such Change Order is agreed, the Change Order shall be signed by both Parties. Upon signature of a Change Order, if Client has not already paid the Manufacturing Slot Deposit for the original Manufacturing Slot, OXB shall re-invoice Client for the applicable deposit for the rescheduled Manufacturing Slot, and Client will pay such Manufacturing Slot Deposit on or before the new Manufacturing Slot Deposit Payment Date.

5.4 Any Manufacturing Slots identified in any executed Scope of Work or Work Order or Change Order shall be binding on both Parties upon signature by both Parties of the Scope of Work or Work Order or Change Order.

5.5 **Cancellation of Reserved Manufacturing Slots**.

(a) Client may cancel any Manufacturing Slot [***] by written notice to OXB at any time prior to the applicable Manufacturing Slot Deposit Payment Date. In the event of cancellation of a Manufacturing Slot by Client pursuant to this clause 5.5(a), Cancellation Charges shall not be payable with respect to the cancelled Manufacturing Slot. For the avoidance of doubt, notwithstanding cancellation of a Manufacturing Slot pursuant to this clause 5.5(a), the applicable Manufacturing Slot Deposit shall be payable by Client by the Manufacturing Slot Deposit Payment Date.

(b) OXB may cancel any Manufacturing Slot [***] by written notice to Client at any time after the applicable Manufacturing Slot Deposit Payment Date in the event that Client has not paid the applicable Manufacturing Slot Deposit by the Manufacturing Slot Deposit Payment Date. In the event of cancellation of a Manufacturing Slot by OXB pursuant to this clause 5.5(b), Client may, at OXB's sole discretion, be charged the Cancellation Charges in accordance with clause 7.5 in addition to the Manufacturing Slot Deposit.

(c) If:

(i) Client terminates the Agreement for any reason other than pursuant to clauses 17.3 (for OXB's breach or insolvency) or 18.1 (for force majeure); or

(ii) Client cancels any Manufacturing Slot other than pursuant to clause 5.5(a) or 5.6 or where OXB expressly agrees that Client is permitted to cancel the Manufacturing Slot without liability for Cancellation Charges under the applicable Scope of Work or Work Order;

then Client will notify OXB in writing [***] and Client may, at OXB's sole discretion, be charged the Cancellation Charges in accordance with clause 7.5 in addition to the Manufacturing Slot Deposit.

5.6 **Supply Failure**.

(a) [***].

(b) [***].

(c) [***]:

(i) [***]; and

(ii) [***];

[***].

(d) [***].

6. Delivery and Defective Batches

6.1 **Terms of Delivery**. OXB shall deliver the Batches Ex Works (INCOTERMS 2020*)* the Facility. OXB shall notify Client confirming the Actual Delivery Date and place of Delivery at least [***] prior to Delivery. Client shall retain, or shall require its carrier to retain, all temperature records in relation to all Batches Delivered from the point of Delivery.

6.2 **Failure to take Delivery**: If Client fails to take actual delivery of any Batch on the Actual Delivery Date and prior arrangements to store such Batch have not been agreed to between the Parties in writing, OXB shall store such Batch on behalf of Client in accordance with the Storage Guidelines, and Client shall be invoiced on the [***] following the Actual Delivery Date for reasonable administration and storage costs. Client agrees that: (i) Client has made a fixed commitment to purchase such Batch; and (ii) except for loss due to negligence, wilful misconduct or breach of this Agreement by OXB, risk of loss for such Batch passes to Client with effect from Delivery.

6.3 **Title**. Title to the Vector shall pass to Client on Delivery.

6.4 **Risk**. Subject to clause 6.2, risk in the Batches shall pass to Client on Delivery.

6.5 **Delivery of Samples**. If Client requires Samples to be shipped separately from any Batch, OXB will ship such Samples as directed by Client Ex Works (INCOTERMS 2020*)* the Facility. OXB shall notify Client of the date on which the Samples will be ready for collection and the place of Delivery at least [***] prior to making them available for collection. Within [***] following completion of any study or assay, unless

OXB has previously agreed in writing to transfer any remaining unused materials to Client at Client's cost, OXB will discard or destroy any remaining unused material, provided such unused material is not required by cGMP to be retained, at Client's request and expense.

6.6 **Quality Assurance**. OXB's quality assurance team ("**Quality Assurance**") shall monitor OXB's activities under this Agreement and in accordance with Applicable Law and the Quality Agreement. All relevant test results and copies thereof shall be provided to Client with the Batch Documentation in accordance with the Quality Agreement. In-process testing results however may be provided to Client before the Batch is completed. Client (or a Third Party designated by Client) shall be solely responsible for releasing any Batch for Development or Commercialisation. Client (in its sole discretion) shall determine the form and substance of any release testing information that is in the Specifications for submission to a regulatory authority. OXB shall provide to Client or to a designated Third Party a Quality Assurance-reviewed and signed OXB Certification within [***] after review and release of the Batch by OXB to Client. OXB shall provide Client via a file share or such other method mutually agreed by the Parties with copies of Master Batch Records for each Batch within [***] after review and release of such Batch by OXB to Client, unless otherwise set forth in the Quality Agreement.

6.7 **Inspection; Release**. OXB will inspect and release or reject (a) Client Materials and Components for use in the Services and (b) the Batches Manufactured pursuant to this Agreement; provided that Client shall be solely responsible for releasing Licensed Product for Development and Commercialisation. OXB shall not use any Client Materials or Components in its performance of the Services that do not conform to the Specifications or are otherwise noticeably damaged, visibly defective, or known to be adulterated. Client may, in conjunction with OXB, inspect and release or reject all Batches Manufactured pursuant to this Agreement. Such inspection and release or rejection by Client may take place on-site at the Facility or at another location agreed upon by the Parties (for example, if Master Batch Records are made available to Client at a location other than the Facility).

6.8 **Acceptance/Rejection; Defective Batches**.

(a) Client shall inform OXB promptly upon discovery of any Defective Batch, but no later than:

(i) [***] after the Actual Delivery Date of such Batch in the event of defects reasonably apparent on visual inspection, without unpacking the Batch; and

(ii) [***] after the date of discovery in the case of defects present at the time of Delivery but not reasonably apparent on visual inspection.

(b) If Client believes that a Batch Delivered by OXB is a Defective Batch and provides notification in accordance with clause 6.8(a), OXB shall promptly conduct an investigation with the aim of determining: (x) whether the Batch is a Defective Batch, (y) the cause of the defect and (z) corrective measures to be taken in the Manufacture of future Batches to minimize changes of or prevent the same cause from happening again. OXB shall promptly advise the Steering Committee of the findings and outcome of such investigation.

(c) If the Parties disagree as to whether a Batch Delivered by OXB is a Defective Batch, they shall submit samples of the Batch and the associated Batch records

(insofar as such Batch records are necessary to enable the Testing Laboratory to perform its analysis), to the Testing Laboratory, which shall carry out tests to determine whether the Batch is a Defective Batch. The Parties shall act in good faith and co-operate with the Testing Laboratory in its investigation. Except in the case of manifest error on the face of its report, the findings of the Testing Laboratory shall be binding on the Parties. The fees of the Testing Laboratory shall be paid by Client unless Batch is a Defective Batch which is not caused by a defect in Client Materials or Client Confidential Information or otherwise by Client, in which case the fees shall be paid by OXB.

(d) If OXB agrees, or the Testing Laboratory (pursuant to clause 6.8(c)) determines that the Batch is a Defective Batch, OXB and Client shall work together to devise appropriate measures to avoid future Batches suffering from such defect. If the Parties agree that a Batch is a Defective Batch, or the Testing Laboratory pursuant to clause 6.8(c) determines that the Batch is a Defective Batch, OXB will replace such Defective Batch in accordance with the following:

(i) to the extent the Defective Batch has resulted from:

(A) failure to Manufacture in accordance with cGMP, the Quality Agreement or Applicable Law; or

(B) failure to conform to the Specifications as a result of negligence or wilful misconduct on the part of OXB or its Affiliates, an act or omission of OXB or its Affiliates which does not meet the standard of skill and care that would reasonably be expected of a reasonable contract manufacturing organization skilled in the art, or failure of equipment, fixtures, facilities and supplies within OXB's reasonable control;

then OXB shall be responsible for the cost of replacing the Defective Batch with a non-Defective Batch, including the costs for transportation, testing and disposal (as applicable), but, except to the extent the Defective Batch resulted from negligence or wilful misconduct on the part of OXB or its Affiliates, excluding costs in relation to Client Materials required for the replacement Batch which shall be provided at Client's cost and expense; and

(ii) in all other circumstances Client shall be responsible for the costs of replacing a Defective Batch, including the costs of transportation, testing and disposal (as applicable) and Client Materials required for the replacement Batch.

(e) OXB shall complete such replacement as soon as reasonably practicable after receipt of the necessary Client Material, and where appropriate following investigation of the cause of the defect and the implementation of appropriate measures to remove such cause, and the Parties shall agree on a revised delivery date for such replacement of the Defective Batch based on the next available Manufacturing Slot. OXB will make reasonable commercial efforts to facilitate timely Delivery of replacement Batches.

(f) Each Party shall destroy the Defective Batch in its possession or control upon the request of the other Party. Such destruction shall be at OXB's cost.

6.9 **Remedies**. Except with respect to OXB obligations of confidentiality and indemnification obligations or OXB's gross negligence or wilful misconduct, Client agrees that its sole remedy with respect to a Defective Batch is as set forth in clause 6.8 and Client hereby waives all other remedies at law or in equity regarding such Defective Batch.

7. Price and Payment

7.1 **Initial Fee**. In partial consideration for the rights and licences granted to Client under this Agreement in relation to the Initial Target, Client shall pay to OXB a one-time, non-refundable, non-creditable upfront payment as set out in Schedule 2 within [***] of the execution of this Agreement.

7.2 **Additional Target Fee**. In partial consideration for the rights and licences granted to Client under this Agreement in relation to any Additional Target included as a Target pursuant to clause 2.4, Client shall pay to OXB a non-refundable, non-creditable payment identified in Schedule 2 (each, an "**Additional Target Fee**") in respect of each such Additional Target within [***] of receipt of OXB's consent pursuant to clause 2.4 in relation to such Additional Target.

7.3 **Service Fee**. Client shall pay the Service Fees set out in the Scope of Work. Unless agreed otherwise by the Parties, [***] of the Service Fee allocated to any Scope of Work, Change Order or Work Order thereto shall be payable upon the start date for the applicable Work Package specified in such Scope of Work, Change Order or Work Order and the remaining [***] payable upon completion of the Work Package.

7.4 **Batch Fee**. Client shall pay to OXB the applicable Batch Fee for each Batch in accordance with the payment schedule set out in Schedule 1. To the extent specified in an applicable Scope of Work or Work Order or Change Order, additional charges may be applied, for example for performance of Manufacturing processes or analytics which are not usually performed by OXB and costs of media validation studies where a filling process or container are required that are not encompassed under existing OXB media validations. A list of the items included in, and a nonexclusive list of items excluded from, the Batch Fee for each Batch is also shown in Schedule 1.

7.5 **Batch Cancellation Charges**.

(a) Where requested by OXB in accordance with clause 5.5(b) or clause 5.5(c), Client shall pay to OXB, in addition to the Manufacturing Slot Deposit, the Cancellation Charges in accordance with Schedule 1.

(b) Except in cases in which Client cancelled pursuant to clause 5.5(a), 5.6, 17.3 or 18.1, if OXB has purchased Components or incurred non-cancellable Pass-Through Costs for any cancelled Manufacturing Slot(s), which Components (and/or items/services the subject of the Pass-Through Costs) cannot be used for other Manufacturing Slots taking into account any applicable shelf-life, the cost of such Components and/or Pass-Through Costs shall be paid by Client to OXB.

(c) Notwithstanding anything in this clause 7.5 to the contrary, in no circumstances shall Client be obliged to pay more in Cancellation Charges and forfeited deposit than it would have paid for the cancelled Batch if the same had not been cancelled.

(d) Notwithstanding the foregoing, if OXB is able to fill the cancelled Manufacturing Slot with a new reservation for another project or customer which was not reserved or contemplated at the time of Client's cancellation, OXB shall reduce the applicable Manufacturing Slot Deposit and Cancellation Charges by deducting the amount received by OXB in respect of such new reservation (but excluding from the deduction (i) any part-payment of such amount received as a deposit in respect of such new reservation and (ii) any out-of-pocket costs incurred by OXB in accomplishing such new reservation). For the avoidance of doubt, this shall not reduce Client's liability for the cost of Components or incurred non-cancellable Pass-Through Costs.

7.6 **Annual Price Adjustments**. OXB may increase the Batch Fee and/or Service Fees and its FTE rate annually with effect from [***], provided that any increase shall be not more than the lesser of (i) [***]during the previous [***] and (ii) [***]. OXB shall inform Client of any price adjustment in writing with [***] prior notice and any such increases shall not apply to any Work Order(s) executed prior to the date of such increase. If publication of the [***]ceases, or if the [***]otherwise becomes unavailable or is altered in such a way as to be unusable, the Parties shall agree on the use of an appropriate substitute [***].

7.7 **Component Costs**. Commencing [***] and no more than once in any [***] period, if the cost to OXB of any Components increases as a result of market conditions including currency fluctuations, so that the cost of any Component increases by [***] or more, then OXB may, by [***] written notice to Client (such notice to include a summary of details of such change) adjust the then-current Batch Fee for future Batches to the extent necessary to cover the increase in cost. OXB shall provide Client with reasonable documentation supporting such increases in costs. For clarity, any such increase in the Batch Fee shall apply solely to Batches the subject of Work Orders placed after the date of such written notice.

7.8 **Development Milestones per Target**. Client shall pay the Development Milestone Payments [***] as set out in Schedule 2 upon the achievement of the Development Milestones.

7.9 **Regulatory Milestones**. Client shall pay the Regulatory Milestone Payments [***] as set out in Schedule 2 upon the occurrence of the Regulatory Milestones.

7.10 **Technology Transfer Milestones**. Client shall pay the Technology Transfer Milestone Payments per Vector as set out in Schedule 2 upon the occurrence of the Technology Transfer Milestones with respect to the relevant Vector.

7.11 **Commercial Milestones**. Client shall pay the Commercial Milestone Payments [***] as set out in Schedule 2 upon the occurrence of the Commercial Milestones.

7.12 **Royalty Payments**. In further consideration of the rights and licences granted to Client hereunder (and if applicable, to Client's Affiliate or a Third-Party manufacturer following Technology Transfer), Client shall pay to OXB during the Royalty Term a royalty on Net Sales at the applicable percentage set out in the table as set out in Schedule 2 (the "**Royalties**"). Client shall, subject to the other terms and conditions of this Agreement, pay OXB the Royalties on annual worldwide Net Sales at the applicable percentage as set out above on a Licensed Product-by-Licensed Product and country-by-country basis during the applicable Royalty Term.

7.13 **Royalty Statements**. Within [***] after the end of each calendar quarter, in respect of Net Sales recorded by any Related Party during that calendar quarter, and within [***]

after the termination of this Agreement, Client shall send to OXB a royalty statement setting out in respect of each Related Party:

(a) in respect of each country in which Licensed Products are sold:

(i) the types of Licensed Products sold in that country;

(ii) the quantity of each Licensed Product sold in each country; and

(iii) the total Net Sales of the Related Party (as applicable) in both USD and the currency in which the Net Sales were recorded showing the conversion rates used broken down by Licensed Product; and

(b) the resulting amount payable by Client, in USD, in respect of Royalties.

7.14 **Payment Terms**.

(a) For all payments due under this Agreement, OXB shall provide Client with an invoice for the amount due. Such invoices shall be sent to the following address:

[***]

or such other address as may be requested by Client from time to time by notice in writing. All invoices must contain:

(i) OXB's name and address;

(ii) the relevant purchase order number, if applicable;

(iii) OXB's VAT number, if applicable; and

(iv) OXB's bank account information.

(b) Client shall pay all amounts in such invoices within [***] of the receipt of such invoice, unless otherwise agreed upon in writing by the Parties (or as expressly set forth in this Agreement with respect to payment of Manufacturing Slot Deposits); provided that if Client reasonably disputes any portion of an invoice, then Client shall pay the undisputed amounts and provide written notice of the disputed amounts and details of the dispute to OXB within [***] of the receipt of such invoice. The Parties shall promptly negotiate in good faith with a view to resolving such dispute and the disputed amount shall not become due until resolution of the dispute.

(c) All sums due to OXB under this Agreement:

(i) are exclusive of Value Added Tax, which where applicable will be paid by Client in addition. OXB shall provide to Client all customary receipts for payment of such taxes and cooperate with Client in making applications for and securing any available exemptions or reductions of VAT reasonably available;

(ii) unless an alternative currency is specified on any invoice, shall be paid in USD in relation to Royalties, the Initial Fee, Additional Target Fees, and Milestone Payments and paid in GBP in relation to all other

payments, in each case by transferring an amount in aggregate to the account identified on the applicable invoice;

(iii) if Licensed Products are sold or supplied by Client or its sublicensees in a currency other than USD (or its successor), the Royalties payable in respect of such sales under this Agreement shall be first determined in the currency of the country in which such sales took place and then converted into USD (or its successor) at the mid rate applicable the invoice date using the OANDA Forex currency converter or other reputable currency converter agreed between the Parties from time to time;

(iv) if laws or regulations require withholding by Client of any taxes imposed upon OXB on account of any royalties and payments paid under this Agreement, such taxes shall be deducted by Client as required by law from such remittable royalty and payment and shall be paid by Client to the proper tax authorities. Official receipts of payment of any withholding tax shall be secured and, upon request, a copy sent to OXB as evidence of such payment. The Parties shall cooperate to ensure that any withholding taxes imposed are reduced as far as possible under the provisions of any relevant tax treaty which shall include providing assistance with the completion of any required forms; and

(v) shall be made by the due date in accordance with clause 7.14(b); provided that any payment which falls due on a date which is not a Business Day in the location from which the payment will be made may be made on the next succeeding Business Day in such location.

(d) If any undisputed payment is not made within [***] after the due date, OXB may charge interest on any outstanding amount of such payment on a daily basis at a rate equivalent to [***] above the base rate of the Bank of England then in force in London, or the maximum rate allowed by Applicable Law if lower.

8. Financial Records and Audit

8.1 **Client Payment Records**. Client shall and shall procure that its Affiliates and sublicensees shall, keep at its or their normal place of business detailed and up-to- date records and accounts in accordance with generally accepted accounting standards as consistently applied in relation to Net Sales, Royalties and Milestone Payments due under this Agreement (as applicable) (the "**Payment Records**"), in each case for at least [***] following the calendar quarter to which they pertain. Such records shall be in sufficient detail to enable OXB to verify the matters to which they pertain.

8.2 **OXB Audit Rights**.

(a) OXB may, upon [***] prior written notice to Client, appoint an internationally-recognised independent accounting firm (which is reasonably acceptable to Client) (the "**Auditor**") for the purpose of verifying the accuracy of any financial statement or report given OXB under this Agreement. OXB shall ensure that any such Auditor be subject to obligations of confidentiality as least as stringent as those provided in this Agreement and that such Auditor keep confidential all information reviewed during such audit. The Auditor shall disclose to OXB and Client its conclusions regarding any payments owed under this Agreement, but not the underlying financial records.

(b) Client and its Affiliates and sublicensee shall make their Payment Records available for inspection by such Auditor during regular Business Day hours at such place or places where such records are customarily kept, upon receipt of [***] prior written notice from OXB. Such records shall be reviewed solely to verify the accuracy of any statement or report given to OXB under this Agreement for any period within the preceding [***]. Such inspection right shall not be exercised [***], unless otherwise agreed in writing. OXB agrees to hold in strict confidence all information received and all information learned in the course of any audit or inspection, except to the extent necessary to enforce its rights under this Agreement, or if disclosure is required by law, regulation or judicial order as set forth in Article 14 (Confidentiality).

(c) In the event that the inspection reveals an underpayment or overpayment by Client, the underpaid or overpaid amount shall be settled promptly and in any event within [***] of the issue of the final report.

(d) OXB shall be responsible for the Auditor's charges and expenses unless the Auditor certifies that there is an under-reporting and underpayment by Client of more than [***] in aggregate amounts payable for any Year, in which case Client shall pay the Auditor's charges and expenses in respect of that inspection.

9. Access to OXB Information

9.1 **OXB Service Records**. OXB will keep appropriate and accurate records (including Batch manufacturing records, testing, cleaning and sterilization records and stability data) of all work done by it under this Agreement, in form and substance as specified in the applicable Scope of Work, Work Package, Work Order, the applicable Quality Agreement, and this Agreement (collectively, the "**Records**"). Records will be available at reasonable times for inspection, examination and copying by or on behalf of Client. All original Records of the Services and Manufacture of Vector under this Agreement will be retained and archived by OXB in accordance with cGMP (if applicable) and Applicable Law, but in no case for less than a period of [***] following completion of the applicable Scope of Work or Work Order.

9.2 OXB shall provide Client, at Client's reasonable request, with copies of such documents, and access to such data and information, including source data and information, in OXB's possession or control as may be necessary for Client to obtain or maintain Regulatory Approval(s) for Licensed Products or respond to Regulatory Authority requests. The actual and reasonable cost of providing such copies and access shall be borne by Client, unless such request results from a finding that OXB's performance of its obligations under this Agreement has been materially deficient, in which case it shall be borne by OXB.

10. Quality Audits and Inspections

10.1 **Facility Audits**.

(a) Subject to OXB's safety procedures, access control SOPs, and confidentiality obligations to other clients, OXB will permit Client's representatives, to conduct a routine audit of any OXB Facility as more specifically set forth in the applicable Quality Agreement, such audits to be carried out in a manner that minimises any interference with OXB's normal operations.

(b) Client may conduct additional for-cause audits of any OXB Facility, as more specifically set forth in the Quality Agreement.

(c) During any audit of an OXB Facility, Client will comply with all reasonable instructions from OXB in relation to health and safety, compliance with cGMP procedures and confidentiality.

(d) The cost of all OXB Facility audits by Client of OXB shall be borne by Client, provided that, in the event that the audit identifies a material deficiency in OXB's performance of its obligations under this Agreement, OXB shall bear its costs of the audit and Client's reasonable out-of-pocket costs.

10.2 **Regulatory Inspections**.

(a) OXB shall permit inspections by Regulatory Authorities relating to the Vector or the Process and shall co-operate with Client for any such inspections in accordance with the provisions of the Quality Agreement.

(b) Except to the extent the inspection identifies a material deficiency in OXB's performance of its obligations under this Agreement (in which case OXB shall bear its costs of the inspection and Client's reasonable out-of-pocket costs), the cost of regulatory inspections of the Facilities that relate solely to the Vectors or Licensed Product shall be borne by Client and will include, without limitation, OXB or its subcontractors' preparation time, costs of external consultants engaged by OXB or its subcontractors to advise on inspection preparation, the costs associated with mock audits, and costs associated with Manufacturing Slots that cannot be used by OXB or its subcontractors due to an inspection, mock inspection or inspection preparation.

11. Regulatory Approvals; Regulatory Matters

11.1 OXB represents and warrants that it holds, and/or will require that its Approved Subcontractors hold, all necessary registrations, permits and licences for any and all Manufacture of Vector by OXB or such Approved Subcontractors under this Agreement from the Regulatory Authorities of the country or countries where such Manufacture takes place. OXB shall comply with all requirements of such registrations, permits and licences. For the avoidance of doubt, Client shall be responsible for all necessary licences and permits required for export/import of Vector.

11.2 Client shall be responsible for obtaining all such registrations, permits and licences as any Regulatory Authority may require it to hold in order to allow Client to Develop or Commercialise the Batches as anticipated under this Agreement.

11.3 Each Party shall make all necessary filings, and respond to any requests for information from Regulatory Authorities, relating to any Regulatory Approvals relating to the Vectors or their Manufacture for which such Party is responsible; provided however, that Client shall control all applications, filings and responses with respect to Regulatory Approval of the use of any Vector or any Licensed Product and that OXB shall provide information in relation to such applications, filings and responses as reasonably required by Client to the extent that OXB is able to do so whilst respecting the confidential information of OXB clients and the Confidential Information of OXB. To the extent OXB is required to make any such filings or responses, prior to making any filing or submitting any response, as applicable, OXB shall provide to Client a copy of the applicable filing or response for review, where possible, respecting the confidential information of OXB clients and the Confidential Information of OXB and take into good faith consideration Client's comments to same. Where a Regulatory Authority has reasonably requested information which cannot be provided by OXB

under this clause 11.3 due to the confidential nature of the information then OXB shall provide that information directly to the relevant Regulatory Authority.

11.4 It shall be Client's responsibility to submit, and Client shall control the submission of, details of any changes to the Manufacturing process to the appropriate Regulatory Authorities and to obtain any necessary approval of such changes, provided that OXB will reasonably cooperate with Client, at Client's cost, with respect to these changes and will provide Client with all information reasonably necessary so that Client can respond to inquiries from Regulatory Authorities and meet its regulatory obligations.

11.5 Client may communicate with any Regulatory Authority about the Vectors or any Services directly, whether or not such communication is necessary to comply with the provisions of this Agreement or any Applicable Laws. OXB shall not communicate with any Regulatory Authority about the Vectors or any Services unless required by Applicable Law or requested to do so by Client, provided that nothing in this Agreement shall prevent OXB from communicating with any Regulatory Authority in relation to any matters which do not specifically relate to a Vector or the Services, including communication relating to OXB's platform. Each Party shall, to the extent permitted by Applicable Law, promptly notify the other Party of any such communication received from any such Regulatory Authority relating to any Vectors or Services. OXB shall fully cooperate with Client in relation to Client's communication with any Regulatory Authority relating to Vectors or the Services, allow any inspection required by any Regulatory Authority relating to Vectors or the Services, allow Client to be present at and participate in any such inspection to the extent permitted by Applicable Law, and fully cooperate with any such inspection to the extent required by Applicable Law.

12. Intellectual Property

12.1 **Ownership of Background IPR**. Nothing in this Agreement will affect either Party's ownership of its Background IPR or any Intellectual Property Rights therein. No licence to use any such Background IPR or Intellectual Property Rights is granted or implied except as expressly set out in this Agreement.

12.2 **Licence to Client**.

(a) OXB hereby grants to Client as of the Effective Date a non-exclusive, worldwide, sublicensable (in accordance with clause 12.6), royalty-bearing (in accordance with clause 7.12) licence under the OXB IP solely to research, Develop and Commercialise the Licensed Products targeting the Initial Targets. For the avoidance of doubt, the foregoing licence shall not include any right to use the OXB IP to manufacture or have manufactured the Vectors and, except with respect to any Licensed Know-How that Client (as the Receiving Party thereof) can prove by means of reasonable written evidence falls within the exceptions described in clause 14.4, Client shall not (other than pursuant to clause 12.3) use the OXB IP to manufacture or have manufactured the Vectors.

(b) OXB shall, and hereby does, grant to Client a non-exclusive, worldwide, sublicensable (in accordance with clause 12.6), royalty-bearing (in accordance with clause 7.12) licence under the OXB IP, in each case solely to research, Develop and Commercialise the Licensed Products targeting any Additional Target, provided that such licence shall only become effective on the date such Additional Target is deemed to be a Target pursuant to clause 2.4 and is subject to payment of the Additional Target Fee with respect to such Additional Target. For the avoidance of doubt, the foregoing licence shall not include any right to use the OXB IP to manufacture or have manufactured the Vectors and,

except with respect to any Licensed Know-How that Client (as the Receiving Party thereof) can prove by means of reasonable written evidence falls within clause 14.4, Client shall not (other than pursuant to clause 12.3) use the OXB IP to manufacture or have manufactured the Vectors.

(c) For clarity, the license grants in clause 12.2(a), clause 12.2(b) and clause 12.3 do not include any rights with respect to any Manufacturing processes other than the Processes. Client shall notify OXB in writing in the event it wishes to licence the TRiP system. The Parties shall negotiate and agree the applicable percentage of royalty on Net Sales for such licence and the table of royalties as set out in Schedule 2 shall be updated accordingly, following which OXB shall grant to Client an additional non-exclusive, worldwide, sublicensable (in accordance with clause 12.6), royalty-bearing (in accordance with clause 7.12) licence under the OXB IP covering the TRiP system solely to research, Develop and Commercialise the Licensed Products.

12.3 **Licence to Client following Technology Transfer**. Effective following Technology Transfer with respect to any Vector pursuant to Article 13, OXB hereby grants to Client a non-exclusive, worldwide, non-sub-licensable, royalty-bearing (in accordance with clause 7.12) licence under the OXB IP, solely for the purpose of manufacturing the applicable Vector using the Process (as such Process may subsequently be modified by Client or, if applicable pursuant to clause 13.2, Client's Affiliate or Third- Party designee after the Technology Transfer; but for clarity, the foregoing shall not be deemed to grant to Client, Client's Affiliate or Third-Party designee a licence with respect to such modified Process under any OXB IP that was not used or incorporated in the original Process that was provided through Technology Transfer pursuant to Article 13) at a facility owned or controlled by Client for use in Licensed Products and researching, Developing and subsequently Commercialising the respective Licensed Products. In no event shall this licence include the right for Client to provide manufacturing services to a Third Party, or to use OXB IP in connection with products or vectors other than the Vectors with respect to which Technology Transfer has occurred pursuant to Article 13.

12.4 **Licence to OXB**. Client hereby grants to OXB a non-exclusive, worldwide, royalty- free licence under the Intellectual Property Rights subsisting in Client's Background IPR and the Client Arising IPR during the Supply Term for the sole purpose of performing OXB's obligations under this Agreement. Such licence shall expire upon the completion of such obligations or the termination or expiration of this Agreement, whichever is the first to occur.

12.5 **Arising IPR**. Any Arising IPR generated by or on behalf of OXB in the performance of this Agreement which: (a) relate solely and exclusively to the GOI or to Client Background IPR provided to OXB for the purposes of this Agreement; or (b) consist solely and exclusively of an improvement to or modification of Client Materials which are proprietary to Client, or (c) require the use of Client Materials which are proprietary to Client or Client's Confidential Information, shall be owned by Client (collectively "**Client Arising IPR**"). Any other arising Intellectual Property Rights generated by or on behalf of OXB in the performance of this Agreement shall remain owned by OXB ("**OXB Arising IPR**"). OXB hereby assigns all right, title and interest in and to Client Arising IPR to Client. OXB agrees to execute such documents and perform such other acts as Client may reasonably request to obtain, perfect and enforce such rights to the Client Arising IPR and the assignment thereof. OXB shall ensure that any persons who are not employees of OXB and who are involved in performing the Services that may reasonably be expected to result in the generation of Client Arising IPR or any

other material Arising IPR hereunder are obligated to assign to OXB all Intellectual Property Rights arising from the performance of such Services.

12.6 **Sublicence Rights**. Client may sublicense its rights under clause 12.2 solely to (a) purchasers of the Licensed Product and (b) Development Partners, in each case on terms consistent with the terms of this Agreement.

12.7 **Non-Exclusivity**. Client acknowledges that OXB is in the business of providing services for a variety of organizations other than Client. Accordingly, subject to OXB's obligations of confidentiality and non-use under clause 14 and provided OXB does not infringe any Client Intellectual Property Rights, nothing in this Agreement will preclude or limit OXB from utilising the general knowledge gained during the course of its performance hereunder to perform similar services for other clients. Client further acknowledges and understands that the services provided under this Agreement are not exclusive to Client.

13. Technology Transfer

13.1 **Technology Transfer Events**. Subject to compliance with the terms and conditions of this Agreement, Client may request to OXB in writing, and OXB shall provide, a [***] Technology Transfer on a Vector-by-Vector basis and in accordance with the remainder of this Article 13 as follows:

(a) a Technology Transfer to Client or Client's Affiliate for no cause on satisfaction of the condition set out in paragraph (a) of Schedule 3;

(b) a Technology Transfer to Client, Client's Affiliate or a Third-Party manufacturer for no cause on satisfaction of the condition set out in paragraph (b) of Schedule 3; or

(c) a Technology Transfer to Client, Client's Affiliate or a Third-Party manufacturer on occurrence of one or more events identified in paragraphs (c) and (d) of Schedule 3;

(each a "**Technology Transfer Event**").

13.2 **Technology Transfers to a Client Affiliate or Third Party**. Prior to Technology Transfer to Client's Affiliate or to a Third Party manufacturer in accordance with clause 13.1(a), 13.1(b) or 13.1(c), OXB shall enter into the licence set out in clause 12.3 above directly with such Affiliate or Third Party which shall also include confidentiality obligations no less protective of OXB than those set out in this Agreement. OXB may reasonably reject any of Client's Affiliates or any Third Party proposed by Client in relation to a Technology Transfer if OXB has reasonable concerns that such Affiliate or Third Party (i) will be unable to maintain the confidentiality of, or will make an unauthorized use or disclosure of, OXB's Confidential Information or (ii) will infringe, violate or otherwise misappropriate OXB's Intellectual Property Rights or OXB's technology. In such case, Client shall be obliged to propose a replacement Client Affiliate or Third Party before proceeding with any Technology Transfer to a Client Affiliate or Third Party and the conditions set out in this clause 13.2 shall apply with respect to the proposed replacement.

13.3 **Technology Transfer Support**. OXB shall provide commercially reasonable support through the Technology Transfer to enable Client (or, if applicable pursuant to clause 13.2, Client's Affiliate or Third-Party designee) to replicate the manufacturing Process developed by OXB as part of the Services, and to Manufacture the Vector conforming

to the applicable Specifications. The Technology Transfer shall include SOPs identified in the Batch records and Specifications that are necessary to establish manufacturing of the Vector in accordance with the applicable Process, including proprietary OXB Intellectual Property Rights only to the extent incorporated into any Process developed for the Manufacture of the Vector pursuant to this Agreement. For clarity, OXB will not provide designs, specifications, and SOPs that are not specifically applicable to the Process or the Vector or that otherwise relate generally to the operation of any of its facilities and/or equipment unless and to the extent reasonably necessary to effect the provisions of this Article 13.

13.4 **Technology Transfer Plan**. Prior to initiating Technology Transfer, the Parties shall agree a Technology Transfer plan without undue delay (and in any case within [***]) following Client's request, which will set out the respective responsibilities of the Parties relating to all aspects of Technology Transfer, including the budget agreed by the Parties. The Technology Transfer costs will include all costs pre-approved by Client as set out in the Technology Transfer plan or otherwise agreed in writing (or included in such budget) and incurred by OXB in connection with Technology Transfer, including Pass-Through Costs and FTE costs. The Technology Transfer plan will also set out the criteria for completion of the Technology Transfer, which criteria shall be agreed by both Parties.

13.5 **Consideration for Technology Transfer**. As consideration for the Technology Transfer described in this Article 13, Client will pay OXB the costs agreed between the Parties and identified in the Technology Transfer plan along with the Technology Transfer Milestone Payments set out in Schedule 2 and, during the applicable Royalty Term, Royalties on annual worldwide Net Sales after the Technology Transfer at the applicable percentage set out in the table as set out in Schedule 2 in accordance with clause 7.12.

13.6 **Cell Lines**. If OXB, as part of Technology Transfer, makes available to Client (or, if applicable pursuant to clause 13.2, Client's Affiliate or Third-Party designee) any Third-Party Cell Lines or other physical materials relating to the Process, Client acknowledges and agrees that Client (or such Affiliate or Third-Party designee) may need to obtain a licence to use such cell lines or physical materials from a Third Party to use such cell lines or other physical materials to manufacture the Vector in accordance with the applicable Process after the Technology Transfer; provided that, except with respect to Third-Party Cell Lines that Client requests in writing OXB to use with respect to the Process, OXB shall have identified in Schedule 6 or the applicable Scope of Work or Work Order all such Third-Party Cell Lines and other physical materials.

14. Confidential Information

14.1 **Duty of Confidence**. Each Receiving Party shall:

(a) keep the Confidential Information of the Disclosing Party secret and confidential at all times;

(b) not disclose or permit the disclosure of any Confidential Information of the Disclosing Party, in whole, in part, or in summary, to any person or entity, except as expressly permitted by this Agreement or the Quality Agreement;

(c) not use the Confidential Information of the Disclosing Party or permit it to be used, in whole or in part, for any purpose other than performance of the

obligations and enjoyment of the rights granted under this Agreement or the Quality Agreement; and

(d) inform the Disclosing Party immediately if it becomes aware of the possession, use or knowledge of any of the Confidential Information of the Disclosing Party by an unauthorised person, and to provide any assistance in relation to such unauthorised possession, use or knowledge that the Disclosing Party may reasonably require.

14.2 **Representatives**. The Receiving Party shall permit access to the Confidential Information of the Disclosing Party only to those of its directors, officers, employees, consultants and contractors, advisors ("**Representatives**") and in the case of OXB, Approved Subcontractors, who:

(a) reasonably require such access for the performance of the obligations and/or enjoyment of the rights granted under this Agreement;

(b) have been informed of the confidential nature of such Confidential Information and the Disclosing Party's interest in such Confidential Information; and

(c) have entered into legally binding confidentiality obligations to the Receiving Party on terms that are no less onerous than those set out in this Agreement, and which extend to such Confidential Information.

save that all information in respect of OXB's manufacturing processes and its business plans disclosed by OXB to Client shall only be disclosed to the directors, officers or employees of Client and not to any other Representatives without the prior written agreement of OXB or such Representative separately executing a confidentiality undertaking directly with OXB consistent with the terms set out in this Agreement.

14.3 The Receiving Party shall ensure that all those persons and entities to whom the Receiving Party has provided access to the Confidential Information of the Disclosing Party comply with the provisions of this Agreement. Notwithstanding any other provision of this Agreement, the Receiving Party shall be liable to the Disclosing Party for any acts or omissions of any such person or entity, that would, if effected by the Receiving Party, constitute a breach of this Article 14.

14.4 **Exceptions**. The Receiving Party's obligations under clause 14.1 shall not apply to any Confidential Information of the Disclosing Party that the Receiving Party can prove by means of reasonable written evidence:

(a) was known to the Receiving Party prior to disclosure by or on behalf of the Disclosing Party and without breach of any confidentiality obligation owed to the Disclosing Party;

(b) is or becomes publicly known other than as a result of breach of this Agreement by the Receiving Party or by anyone to whom the Receiving Party disclosed the Confidential Information of the Disclosing Party;

(c) is received by the Receiving Party from a Third Party lawfully entitled to make the disclosure without restrictions on such Third Party's rights to disclose or use; or

(d) is developed by or on behalf of the Receiving Party without any direct or indirect access to, or use or knowledge of, the Confidential Information of the Disclosing Party, as established by contemporaneous documentary evidence;

except that Confidential Information that is specific and would not by itself fall within the above exceptions does not become included in the above exceptions merely as a result of being embraced by more general information that does fall within the above exceptions.

14.5 **Required Disclosures**. The Receiving Party will not be in breach of its obligations under this Agreement to the extent that it is required to disclose Confidential Information of the Disclosing Party by Applicable Law, including to meet the financial and accounting audit and reporting obligations of a publicly traded company, (provided, in the case of a disclosure under any freedom of information legislation, that the exemptions under that legislation do not apply) or order of a court or other public body or Regulatory Authority or other authority that has jurisdiction over it or pursuant to the rules of any recognized stock exchange, provided that, before making such a disclosure, the Receiving Party shall, to the extent it is legally permitted to do so:

(a) inform the Disclosing Party of the proposed disclosure as soon as possible, and if possible before the court or other public body orders the disclosure;

(b) take into account reasonable requests of the Disclosing Party in relation to such disclosure;

(c) except with respect to public company audit and reporting disclosures, ask the court or other public body to treat such Confidential Information as confidential; and

(d) except with respect to public company audit and reporting disclosures, permit and assist the Disclosing Party to make representations to the court or other public body in respect of the disclosure and/or confidential treatment of such Confidential Information.

14.6 **Additional Disclosures**. In addition to disclosures allowed under clause 14.5:

(a) subject to and in accordance with clause 11.3, OXB shall provide OXB's Confidential Information to Regulatory Authorities as reasonably required by Client in relation to Client's applications, filings and responses with respect to Regulatory Approval(s) for Vectors and Licensed Products;

(b) Client may disclose Confidential Information of OXB to the extent such disclosure is necessary in connection with sublicensing (or potential sublicensing) of the rights granted under this Agreement, provided that such disclosure is made only under obligations of confidence and non-use at least as stringent as set out in this Agreement and that, in relation to the Manufacturing process, only a pre-agreed high level overview may be disclosed. The Parties shall use reasonable efforts to promptly agree on such high-level overview once the Process has been finalised;

(c) OXB may disclose, to its licensor or assignor of Intellectual Property Rights related to this Agreement, financial Confidential Information of Client provided to OXB under this Agreement to the extent required for the specific purpose of enabling OXB to comply with its contractual royalty reporting obligations to any such licensor or assignor of Intellectual Property Rights to OXB; provided that

any such disclosure is made only under obligations of confidence and non-use at least as stringent as set out in this Agreement;

(d) Each Party and its Affiliates may disclose:

(i) the existence of this Agreement, and a redacted version of this Agreement (provided that the other Party is given the opportunity to require a redaction from the Agreement of commercially sensitive terms that are not reasonably necessary for such financial or institutional investors or potential purchasers to conduct a reasonable and customary due diligence of the Agreement, and further provided that any such disclosure is made only under obligations of confidence and non-use at least as stringent as set out in this Agreement) to financial or institutional investors or potential purchasers of the business of such Party or its Affiliates in connection with:

(A) the raising of finance,

(B) the sale of any equity interest in such Party or its Affiliates, or

(C) the sale of the business or relevant part of the business of the Party or its Affiliates, and

(ii) the existence of this Agreement in written materials or oral presentations, provided however, that such materials or presentations accurately describe the nature of this Agreement in a manner consistent with information that has already been publicly disclosed and such information is accurate at the time of disclosure.

14.7 **Return and Destruction of Confidential Information**. At the sooner of: (i) or termination of this Disclosing Party's written request and (ii) on expiration Agreement, the Receiving Party shall:

(a) other than as provided below, immediately destroy or erase all Confidential Information of the Disclosing Party that the Receiving Party has received under this Agreement including any copies made and permanently delete all electronic copies of any such Confidential Information from the Receiving Party's computer systems; and

(b) make no further use of any such Confidential Information,

The Receiving Party may, however, keep one copy of the Confidential Information of the Disclosing Party in its legal files solely for the purpose of enabling it to comply with the provisions of this Agreement, and the Receiving Party shall not be required to remove such Confidential Information of the Disclosing Party from its back-up or archive electronic records including its electronic laboratory notebook and laboratory information management systems. In addition, Client may retain Confidential Information of OXB during any other period in which the licences to Client under clause 12.2 or 12.3 are in effect, solely to the extent that such Confidential Information is necessary or reasonably required for Client to exercise such licence rights.

14.8 **Press Releases and Publicity**. Neither Party shall make, nor permit any person to make, any public announcement, whether oral or written, concerning this Agreement or make any use of the name, symbol, trade mark, trade name or logo of the other Party or its Affiliates without the prior written consent of the other Party (such consent

not to be unreasonably withheld or delayed); provided, however, that (a) notwithstanding any other provision of this Agreement, each Party shall be permitted to make an announcement in the agreed form appended to this Agreement at Schedule 4 and otherwise repeat the information contained therein (or contained in any previous announcement consented to in writing by the other Party) and (b) each Party shall be permitted to make required disclosures pursuant to clause 14.5 (Required Disclosures), and in each case such activities shall not constitute a breach of this Agreement.

15. Indemnities and Liability; Insurance

15.1 **No Exclusion**. Nothing in this Agreement shall exclude or limit, or purport to exclude or limit, a Party's liability in the case of:

(a) wilful misconduct, fraud or fraudulent misrepresentation;

(b) any breach of Article 14 (Confidentiality);

(c) death or personal injury resulting from its negligence;

(d) [***]; or

(e) any other matter in respect of which it would be unlawful to exclude or restrict liability.

15.2 **Limitation of Damages**. Subject to clause 15.1 above, neither Party nor any of its Affiliates shall be liable in contract, tort, negligence, breach of statutory duty or otherwise to the other Party for any consequential, incidental, special, punitive, exemplary or indirect loss or damage, loss of profits, loss of business or loss of goodwill arising out of this Agreement, except to the extent any such damages are required to be paid to a Third Party as part of a claim for which a Party provides indemnification under this Article 15. Subject to clause 15.1 above, the aggregate liability of OXB to Client whether directly or by indemnification shall be limited to an amount equivalent to [***] the amount paid or payable by Client to OXB under the relevant Scope of Work, Change Order or Work Order pursuant to which the cause of action has arisen.

15.3 **Client Indemnity**. Client shall defend, indemnify and hold harmless OXB, its Affiliates and each of their respective officers, directors, employees, contractors and agents (the "**OXB Indemnitees**") from and against any and all Claims against an OXB Indemnitee arising out of:

(a) any claim that Client's supply to OXB of Client's Confidential Information or the Client Materials, or that OXB's use of the same (or OXB's use of a Third Party Cell Line at Client's request) in the performance of the Services during the Supply Term in accordance with the terms of this Agreement infringes or misappropriates the Intellectual Property Rights or other proprietary rights of a Third Party;

(b) the negligence or wilful misconduct of Client or any of its Affiliates;

(c) any breach by Client of any representation, warranty or covenant made by Client in this Agreement or the Quality Agreement; or

(d) the research, development, use, manufacture, distribution, sale or import of any Vector or Licensed Product by Client or its Affiliates, sublicensees or

collaborators, including, but not limited to, any actual or alleged injury or death, claimed to result directly or indirectly from the possession, use or consumption of, or treatment with, any such Vector or Licensed Product;

in each case, except to the extent that such Claim is attributable to:

(i) Delivery by OXB of a Defective Batch which defect was not attributable to (A) a defect in Client Materials that was present at the time of delivery to OXB hereunder but was not reasonably apparent upon inspection by OXB, or (B) Client Confidential Information, and provided that Client did not knowingly use a Defective Batch;

(ii) any breach by OXB of any representation, warranty or covenant made by OXB under this Agreement or the Quality Agreement;

(iii) negligence or wilful misconduct of an OXB Indemnitee; or

(iv) any claims for which OXB has an obligation to indemnify the Client Indemnitees pursuant to clause 15.4.

15.4 **OXB Indemnity**. OXB shall defend, indemnify and hold harmless Client, its Affiliates and each of their respective officers, directors, employees, contractors and agents (the "**Client Indemnitees**") from and against any and all Claims against a Client Indemnitee arising out of:

(a) the negligence or wilful misconduct of OXB or any of its Affiliates; and

(b) any breach by OXB of any representation, warranty or covenant made by OXB under this Agreement or the Quality Agreement;

(c) [***]; and

in each case, except to the extent that such Claim is attributable to:

(i) any breach by Client of any representation, warranty or covenant made by Client under this Agreement or the Quality Agreement; or

(ii) negligence of or wilful misconduct of a Client Indemnitee; or

(iii) any claims for which Client has an obligation to indemnify the OXB Indemnitees pursuant to clause 15.3.

and further provided that, if any IPR Claim is made or is reasonably likely to be made against a Client Indemnitee, OXB may at, its sole option and expense, and Client shall permit OXB to procure for the Client Indemnitee the right to, continue practicing the OXB Manufacturing Process (or any part thereof).

15.5 **Indemnification Procedure**. Where a Party (the "**Indemnified Party**") seeks indemnification from the other Party (the "**Indemnifying Party**") under clause 15.3 or 15.4:

(a) the Indemnified Party shall provide prompt written notice to the Indemnifying Party of the assertion or commencement of any Claim for which it is seeking indemnification; provided, however, that failure to provide such notice shall not

relieve the Indemnifying Party of any of its obligations hereunder except to the extent the Indemnifying Party is prejudiced by such failure;

(b) the Indemnifying Party shall have the right to assume (with its own counsel and at its own costs) the defence and/or settlement of the same; provided that the Indemnifying Party shall not agree to any settlement of such Claim under terms that would require the Indemnified Party to pay any money or admit wrongdoing without the Indemnified Party's prior written approval (such consent not to be unreasonably withheld, conditioned or delayed);

(c) the Indemnifying Party shall not be liable for any settlement made by the Indemnified Party without the Indemnifying Party's prior written consent; and

(d) the Indemnified Party shall:

(i) promptly provide all assistance and information reasonably required by the Indemnifying Party;

(ii) not make any admission of liability, conclude any agreement or make any compromise with any person in relation to such claim, demand, action or suit without the prior written consent of the Indemnifying Party (which consent shall not be withheld unreasonably); and

(iii) have the right to participate in (but not control) the defence of the claim, demand, action or suit and to retain its own counsel in connection with such claim, demand, action or suit at its own expense.

15.6 **Mitigation of Loss**. Each Indemnified Party will take and will ensure that its Affiliates take all such commercially reasonable steps and actions that are necessary or as the Indemnifying Party may reasonably require, in its reasonable discretion, to mitigate any Claims (or potential losses or damages) under this Article 15; it being understood that Client would not be required to cease Development or Commercialisation of the Licensed Product as part of such mitigation efforts. Nothing in this Agreement shall or shall be deemed to relieve any Party of any common law or other duty to mitigate any losses incurred by it.

15.7 **Insurance**.

(a) OXB Insurance. OXB will secure and maintain in full force and effect throughout the term of this Agreement (and for at least [***] thereafter for claims made coverage), the following minimum insurance coverage with financially sound and internationally reputable insurers with a minimum A. M. Best Rating of A-/VII:

(i) Employers' Liability of at least [***];

(ii) Public and Products Liability, including personal/advertising injury, coverage for completed operations, and contractual liability assumed by OXB, with at least [***] combined single limit for bodily injury and property damage per occurrence, and a general aggregate limit of at least [***];

(iii) "All Risk" Property, valued at replacement cost, covering loss or damage to Client's property and materials in the care, custody, and control of OXB whether at the Facility, in transit to the delivery location,

or otherwise with Client named as loss payee for Client's property and materials provided that (A) Client has provided sufficient detail of the relevant property and materials and costs thereof to enable OXB to procure such coverage under its insurance policy and (B) OXB shall be entitled to recharge to Client any cost of procuring such coverage in excess of [***], or Client shall be entitled to insure Client's property and materials under its own insurance coverage.

Liability policies written on a claims-made basis will have a retroactive date no later than the Effective Date of this Agreement. Coverage territory will include claims brought in the United States and worldwide, if applicable.

(b) Client Insurance. Client shall obtain and maintain in full force and effect at all times during the Term and for at least [***] thereafter such types and amounts of insurance with financially sound and internationally reputable insurers with a minimum A. M. Best Rating of A-/VII as is normal and customary for it to cover its indemnification obligations under this Agreement.

(c) Proof of Insurance. Upon request by the other Party, each Party shall procure from its insurance broker a letter confirming the coverage required of such Party under this clause 15.7.

16. Warranties and Representations

16.1 **Mutual Representations and Warranties**. Each Party hereby represents and warrants to the other as of the Effective Date that:

(a) it is a corporation duly organised, validly existing and in good standing under the laws of its jurisdiction of formation;

(b) it has full corporate power and authority to execute, deliver, and perform this Agreement, and has taken all corporate action required by law and its organisational documents to authorise the execution and delivery of this Agreement and the consummation of the transactions contemplated by this Agreement;

(c) all consents, approvals and authorisations from all governmental authorities required to be obtained by such Party in connection with this Agreement have been obtained;

(d) the execution and delivery of this Agreement and all other instruments and documents required to be executed pursuant to this Agreement, and the consummation of the transactions contemplated hereby do not and shall not (i) conflict with or result in a breach of any provision of its organizational documents; or (ii) result in a breach of any agreement to which it is a party; and

(e) (i) neither such Party nor, to the Knowledge of such Party any of its employees or contractors used to perform any Services or other activities in connection with this Agreement, has been debarred under Subsection (a) or (b) of Section 306 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 335a); and (ii) to the Knowledge of such Party, no person on any of the FDA clinical investigator enforcement lists (including, but not limited to, the (1) Disqualified/Totally Restricted List, (2) Restricted List and (3) Adequate Assurances List) will participate in the performance of any activities hereunder, and each Party will promptly notify the other in the event that such Party becomes aware that it or

any of its employees or contractors used to perform any Services or other activities in connection with this Agreement becomes debarred or is added to such lists.

16.2 **Additional Representations and Warranties of OXB**

(a) [***];

(b) [***];

(c) [***];

(d) [***];

(e) [***];

(f) [***];

(g) [***];

(h) [***];

(i) [***]; and

(j) [***].

16.3 **No Other Warranties**. Each of the Parties acknowledges that, in entering into this Agreement, it does not do so in reliance on any representation, warranty, or other provision except as expressly provided in this Agreement, and any conditions, warranties or other terms implied by statute or common law are excluded from this Agreement to the fullest extent permitted by Applicable Law. In particular, other than as expressly provided herein, OXB expressly disclaims all warranties relating to the Vector and the Services including any warranty of satisfactory quality, merchantability, or fitness for any particular purpose.

17. Duration and Termination

17.1 **Term and Duration of Agreement**. This Agreement shall come into effect on the Effective Date and, subject to earlier termination in accordance with this Agreement, and subject to clause 17.7:

(a) with respect to clauses 1.3, 3, 4, 5, 6 and 10 with respect to the performance of Services and the Manufacture and supply of Batches of Vector by OXB to Client, shall continue in effect until the later of (i) [***] from the Effective Date and (ii) the completion of Services under the last Scope of Work, Work Package, Work Order or Change Order, in each case, that was executed by the Parties prior to [***] (the "**Supply Term**"); and

(b) with respect to the remainder of the Agreement, shall continue in force until no further payments are due to OXB under this Agreement (the "**Term**").

Upon expiry of this Agreement pursuant to clause 17.1(b), all licenses granted to Client hereunder shall become perpetual and fully paid-up.

17.2 **Client Termination of Agreement Without Cause**. Client may terminate this Agreement without cause, by giving at least [***] written notice to OXB. In such

circumstances the Cancellation Charges shall apply with respect to all cancelled Manufacturing Slots in accordance with clause 7.5.

17.3 **Termination for Cause**.

(a) If either Client or OXB is in material breach of any material obligation hereunder or under the Quality Agreement, the other Party may give written notice to the breaching Party specifying the claimed particulars of such breach, and in the event such material breach is not cured within [***] where the breach is a failure to make a payment due) after such notice, the notifying Party shall have the right thereafter to terminate this Agreement immediately by giving written notice to the breaching Party to such effect.

(b) Either Party may terminate this Agreement upon written notice to the other Party if an Insolvency Event occurs in relation to the other Party and such Insolvency Event is not dismissed or remedied within [***] after its occurrence. Unless otherwise prohibited by Applicable Laws, in any event when a Party first becomes aware of the likely occurrence of any Insolvency Event in regard to that Party, it shall promptly so notify the other Party in sufficient time to give the other Party sufficient notice to protect its interests under this Agreement.

17.4 **Termination of Work Orders**. Client may terminate any Scope of Work, Work Package or Work Order with or without cause by giving [***] written notice to OXB, and other than with respect to the orderly winddown of any work under such a terminated Scope of Work, Work Package or Work Order within the notice period, OXB shall have no further obligations with respect to such Scope of Work, Work Package or Work Order and shall, upon receipt of such notice, cease all work in respect thereof. If applicable to the cancelled Scope of Work, Work Package or Work Order, Cancellation Charges will apply with respect to all cancelled Manufacturing Slots in accordance with clause 7.5. OXB may invoice Client for: (i) all costs actually and reasonably incurred and non-cancellable costs reasonably committed prior to the effective date of termination in connection with the cancelled Scope of Work, Work Package or Work Order (to the extent such costs are not covered under the costs described in (iii)); (ii) all reasonable and documented costs associated with the wind-down activities in accordance with this clause 17.4; and (iii) Client's liability for all fees and other payments and costs for the Services listed in any relevant Work Package up to the effective date of termination; provided that (A) the amount due from Client under this clause 17.4 shall not exceed the costs set forth in the applicable Scope of Work, Work Order or Work Package and shall exclude any amounts paid or payable by Client pursuant to clause 7.5(b); and (B) OXB shall take reasonable efforts to mitigate and minimize the amount due from Client pursuant to this sentence.

17.5 **Consequences of termination**.

(a) In the event of termination of this Agreement, such termination shall be deemed to be a termination of all outstanding Scopes of Work, Work Packages and Work Orders, subject to clause 17.5(b).

(b) Upon termination of this Agreement:

(i) by either Party for any reason, OXB will complete Delivery of, and Client shall take delivery of, and pay OXB for, all Batches that were completed as of the date of the relevant notice of termination;

(ii) by OXB for Client's uncured breach or insolvency pursuant to clause 17.3, OXB may elect to either cease or continue with the Manufacture of any Batches for which a Work Order had been executed before the effective date of termination or expiry; provided that, (1) to the extent that OXB elects to continue Manufacture and make Delivery of such Batches, Client shall take delivery of and pay OXB for, all such Batches; and (2) to the extent that OXB elects not to continue Manufacture and make Delivery of such Batches, Client shall pay OXB the applicable Cancellation Charges for all Manufacturing Slots which are cancelled as a result; or

(iii) by Client without cause pursuant to clause 17.2 or by Client for OXB's uncured breach or insolvency pursuant to clause 17.3, Client shall instruct OXB in writing at the time of giving notice of termination whether or not OXB should continue with the Manufacture of any Batches for which a Work Order had been executed before the effective date of termination.

(c) Upon termination of this Agreement by either Party for any reason:

(i) Client will pay the Batch Fee for any Batches which have undergone OXB's certification and been delivered in accordance with clause 17.5(b), provided however that clause 6.8 shall continue to apply with respect to any such Batch which is a Defective Batch;

(ii) except with respect to Batches for which a Cancellation Charge has been paid or is payable, where Client instructs OXB to cease Manufacture of Batches pursuant to clause 17.5(b)(iii), or where OXB elects to cease Manufacture pursuant to clause 17.5(b)(ii): (A) Client shall pay OXB all reasonable actually incurred or committed costs up to the date of instruction to cease Manufacture; provided that these costs shall not exceed the costs set forth in the applicable Work Order(s) and shall exclude any amounts paid or payable by Client pursuant to clause 7.5(b) or clause 17.4; and (B) OXB shall take reasonable efforts to mitigate and minimize any such costs; and

(iii) where Client instructs OXB to continue Manufacture of a Batch pursuant to clause 17.5(b)(iii), or where OXB elects to continue Manufacture of a Batch pursuant to clause 17.5(b)(ii), such Manufacture shall be subject to the terms and conditions of this Agreement, including clause 5.6.

(d) Upon termination of this Agreement:

(i) by OXB for Client's uncured breach or insolvency pursuant to clause 17.3 or by Client for convenience pursuant to clause 17.2 or by OXB for force majeure pursuant to clause 18.1, the licences granted to Client under clause 12.2 shall terminate immediately (subject to Client's sell-off rights under this clause) and any licence granted to Client pursuant to clause 12.3 shall terminate immediately; provided however that Client shall be entitled to sell or otherwise dispose of any unsold or unused stocks of Licensed Product for up to [***] after the effective date of termination subject to payment of applicable Royalties for the remainder of the Royalty Term; or

(ii) by Client for OXB's uncured breach or insolvency pursuant to clause 17.3 or by Client for force majeure pursuant to clause 18.1, (1) the licences granted to Client under clause 12.2 shall survive such termination in accordance with their terms until the Term would otherwise expire under Section 17.1; provided that Client continues to pay all Royalties due to OXB pursuant to clause 7.12 during the remainder of the applicable Royalty Term; and thereafter, such license shall become perpetual, irrevocable and fully paid-up for the applicable country; (2) any licence granted pursuant to clause 12.3 or 13.2 shall survive in accordance with its terms provided that Client continues to pay all Royalties due to OXB pursuant to clause 7.12 during the remainder of the applicable Royalty Term, and applicable Technology Transfer Milestone Payments and costs in accordance with clause 13.5; and (3) Client shall have no obligation to pay to OXB any Development Milestone Payments, Regulatory Milestone Payments or Commercial Milestone Payments that were not already due to OXB as of the effective date of termination.

17.6 **Termination Not Sole Remedy**. A Party's right of termination under this Agreement, and the exercise of any such right, shall be without prejudice to any other right or remedy (including any right to claim damages) that such Party may have in the event of a breach of contract or other default by the other Party.

17.7 **Survival**. Expiration or termination of this Agreement shall not relieve the Parties of any obligation accruing prior to such expiration or termination. In addition, the provisions of clauses: 1 (*Definitions and Interpretation)*; 4.2(b) (*Delivery and Title to Client Materials*) and 4.4 (*Import and Export*); 5.5 (*Cancellation of Reserved Manufacturing Slots)*; 6 (*Delivery and Defective Batches)* with respect to Batches delivered prior to termination or expiration of the Agreement or in accordance with clause 17.5(b); 7 (*Price and Payment*), with respect to those payments that accrued prior to termination or expiration of the Agreement or pursuant to clause 17.5; 8 (*Financial Records and Audit*); 9 (*Access to OXB Information*); 11 (*Regulatory Approvals; Regulatory Matters*); 12.1, 12.5 and 12.7 (*Intellectual Property*); 13.5 (*Consideration for Technology Transfer*) with respect to those payments that accrued prior to the effective date of termination or expiration or pursuant to clause 17.5; 14 (*Confidential Information*); 15 (*Indemnities and Liability*); 16 (*Warranties and Representations*); 17.4, 17.5, 17.6 and 17.7 (*Termination)*; and 18 (*General*); shall survive expiration or termination of this Agreement each for the period specified therein, or, if no period is specified therein, then perpetually.

18. General

18.1 **Force Majeure**. Neither Party shall have any liability or be deemed to be in breach of this Agreement for any delays or failures in performance of this Agreement that result from circumstances beyond the reasonable control of that Party and which circumstances are not reasonably foreseeable, including, by way of example and not of limitation, fire, flood, explosion, storm, hurricane, strike, lockout or other labour dispute, riot, war, rebellion, accidents, equipment failure, acts of God, or acts of governmental agencies or instrumentalities. For clarity, COVID-19 conditions as they exist on the Effective Date will not constitute a force majeure condition under this Agreement. The Party affected by such circumstances shall promptly notify the other Party in writing when such circumstances cause a delay or failure in performance and use its reasonable endeavours to avoid or remove the causes of nonperformance and shall continue performance as expeditiously as possible as soon as such causes have been removed. If any circumstances described in this clause 18.1 prevent a Party

from performing its material obligations under this Agreement for [***], the other Party may terminate this Agreement by giving [***] written notice to the affected Party.

18.2 **Compliance with Law**. Each Party shall perform its obligations under this Agreement in accordance with all Applicable Laws. No Party shall, or shall be required to, undertake any activity under or in connection with this Agreement which violates, or which it believes, in good faith, may violate, any Applicable Law.

18.3 **Further Action**. Each Party agrees, without the necessity of further consideration, to execute, acknowledge, and deliver such further instruments, and do all further similar acts, as may be necessary or appropriate to carry out the purposes and intent of this Agreement.

18.4 **Notices and Other Communications**: Any notice to be given under this Agreement must be in writing, and be delivered to the other Party by courier or other recorded delivery post (with an advance copy by email) and will be deemed to be received on the date of delivery. Until changed by notice given in accordance with this clause 18.4, all notices should be addressed as follows:

For OXB:	**For Client:**
[***]	[***]

18.5 **Amendment**. This Agreement may only be amended in writing signed by duly authorised representatives of the Parties.

18.6 **Assignment**. Neither Party may assign, mortgage, charge or otherwise transfer any of its rights nor obligations under this Agreement without the other Party's prior written consent (which consent shall not be unreasonably withheld or delayed), except that either Party may assign its rights and obligations under this Agreement, without the consent of the other Party to any Third Party acquiring all or substantially all of the assigning Party's assets or business to which this Agreement relates, provided that, in all cases:

(a) the assigning Party shall provide the other Party with prompt written notice of any such assignment; and

(b) the permitted assignee shall assume the obligations of the assigning Party hereunder in writing.

18.7 **Third Party Rights**. The provisions of this Agreement are for the sole benefit of the Parties and their successors and permitted assigns, and they shall not be construed as conferring any rights to any Third Party except as otherwise expressly provided in Article 15 above. Except as expressly provided in Article 15 above, no person who is not a Party to this Agreement (including any employee, officer, agent, representative or subcontractor of either Party) shall have the right to enforce any term of this Agreement which expressly or by implication confers a benefit on that person without the express prior agreement in writing of the Parties.

18.8 **Entire Agreement**. This Agreement, including any Scopes of Work, Work Packages, Work Orders and Change Orders hereunder, together with the Quality Agreement and Schedules and Appendices to this Agreement, constitute the entire agreement

between the Parties relating to their subject matter and in relation to such subject matter supersedes all earlier understandings and agreements between the Parties, except with respect to the CDA and FSA (which have been terminated pursuant to this Agreement).

18.9 **Relationship**. Nothing in this Agreement creates, implies or evidences any contract of employment or any partnership or joint venture between the Parties, or authorises either Party to act as agent for the other. Moreover, each Party agrees not to construe this Agreement, or any of the transactions contemplated hereby, as a partnership for any tax purposes. Each Party shall act solely as an independent contractor, and nothing in this Agreement shall be construed to give any Party the power or authority to act for, bind, or commit the other. OXB is acting under this Agreement as an independent contractor. OXB will be responsible for and will withhold and/or pay any and all applicable federal, state or local taxes, payroll taxes, workers' compensation contributions, unemployment insurance contributions, or other payroll deductions from the compensation of OXB's employees and other OXB personnel. OXB understands and agrees that it is solely responsible for such matters and that it will indemnify Client and hold Client harmless from all claims and demands in connection with such matters.

18.10 **Waiver of Rights**. No failure or delay by a Party to exercise any right or remedy provided under this Agreement or by law or to insist upon compliance with any term or condition of this Agreement will constitute a waiver of that (or any other) right or remedy or excuse a similar subsequent failure to perform any such term or condition by the other Party. No waiver shall be effective unless it has been given in writing and signed by the Party giving such waiver. No single or partial exercise of such right or remedy will preclude or restrict the further exercise of that (or any other) right or remedy.

18.11 **Unenforceable Provisions**. If the whole or any part of any provision of this Agreement is unenforceable in any jurisdiction, then this Agreement shall be construed as if such provision were not contained herein and the remainder of this Agreement shall continue in full force and effect. The Parties will use their commercially reasonable efforts to substitute for the invalid or unenforceable provision a valid and enforceable provision which conforms as nearly as possible to the original intent of the Parties. The validity and enforceability of that provision in any other jurisdiction will not be affected.

18.12 **Counterparts**. This Agreement may be executed in any number of counterparts, each of which is an original but all of which together will constitute one document. Electronic or PDF signatures of authorized signatories of any Party will be deemed to be original signatures and will be valid and binding, and delivery of an electronic or PDF signature by any Party will constitute due execution and delivery of this Agreement.

18.13 **Governing Law**. This Agreement and all matters relating to it shall be governed by and construed in accordance with the laws of England and Wales.

18.14 **Dispute Resolution**. Any dispute arising out of or relating to this Agreement shall be subject to the dispute resolution set out in clause 2 and in the event that the Senior Officers are not able to agree either Party may submit to the exclusive jurisdiction of the courts located in London, England. Notwithstanding the foregoing, either Party may seek an interim injunction in any court of competent jurisdiction.

18.15 **Cumulative Remedies**. The rights and remedies in this Agreement are cumulative and not exclusive of any other right or remedy that might be available at law or in equity.

18.16 **Expenses**. Except as otherwise expressly provided in this Agreement, each Party shall pay the fees and expenses of its respective lawyers and other experts and all other expenses and costs incurred by such Party incidental to the negotiation, preparation, execution and delivery of this Agreement.

AGREED by the Parties to this Agreement through their authorised signatories:

For and on behalf of	**For and on behalf of**
OXFORD BIOMEDICA (UK) LIMITED:	**CABALETTA BIO, INC.**
Signature /s/ Jason Slingsby	**Signature** /s/ Steven Nichtberger
Print name Jason Slingsby	**Print name** Steven Nichtberger, M.D.
Job title Chief Business and Corporate Development Officer	**Job title** Chairman and CEO
Date 30 December 2021	**Date** 30 December 2021

SCHEDULE 1

Batch Fee and Cancellation Fees

[***]

SCHEDULE 2

Milestones and Royalties

Fees

Initial Fee (clause 7.1): [***]

Additional Target Fee (clause 7.2): [***]

Development Milestones ([***])

Development Milestone	**Payment (USD) upon achievement of Development Milestone***
[***]	[***]

Regulatory Milestones ([***])

Regulatory Milestone	**Payment (USD) upon achievement of Regulatory Milestone***
[***]	[***]

Commercial Milestones ([***])

Commercial Milestone	**Payment (USD) upon achievement of Commercial Milestone ***
[***]	[***]
[***]	[***]

* Client shall notify OXB as soon as reasonably practicable following the occurrence of each milestone in the milestone tables above. Client shall pay the corresponding amounts set out Biomedical above in respect of that milestone within [***] after receipt of an invoice from OXB for the same. The amount stipulated as payable for each milestone in the milestone tables above shall be payable by Client to OXB the [***]time the applicable milestone is achieved

with respect to each Licensed Product (for the Development Milestones, Regulatory Milestones and Commercial Milestones), whether by Client alone or in combination with or by one or more Affiliates or sublicensees. Where the regulatory process for a Licensed Product is accelerated such that a particular milestone is not required by the relevant Regulatory Authority, the payment in respect of that milestone shall become due and payable upon the occurrence of the next milestone in the table above. All such payments shall be non-refundable.

Technology Transfer Milestones (single, one-time payments on a per Vector basis)

Technology Transfer Milestone	**Payment (USD) upon achievement of Technology Transfer Milestone**
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

** OXB shall notify Client as soon as reasonably practicable following the occurrence of each Technology Transfer Milestone in the milestone table above. Client shall pay the corresponding amounts set out above in respect of that milestone net [***] after receipt of an invoice from OXB for the same. Subject to clause 17.5(d)(ii), Development Milestone Payments, Regulatory Milestone Payments and Commercial Milestone Payments will continue to be owed by Client if and when they are achieved after a Technology Transfer.

Royalties

Royalty rate if Vectors manufactured by OXB	**Royalty rate if Vectors manufactured by Client following Technology Transfer**	**Royalty rate if Vectors manufactured by a Third-Party manufacturer following Technology Transfer**
[***]	[***]	[***]

Oxford Biomedica

SCHEDULE 3

Technology Transfer Events

[***]

SCHEDULE 4

Press Release

Oxford Biomedica Signs Licence and Supply Agreement with Cabaletta Bio for LentiVector® Platform

Oxford, UK - [XX] January 2022: Oxford Biomedica plc (LSE:OXB) ("Oxford Biomedica" or "the Group"), a leading gene and cell therapy group, today announces that it has signed a new Licence and Supply Agreement (LSA) with Cabaletta Bio, Inc. (Nasdaq: CABA) ("Cabaletta Bio"), a Philadelphia, USA-based clinical-stage biotechnology company focused on the discovery and development of engineered T cell therapies for patients with B cell- mediated autoimmune diseases. The LSA grants Cabaletta Bio a non-exclusive license to Oxford Biomedica's LentiVector® platform for its application in Cabaletta Bio's leading Chimeric AutoAntibody Receptor (CAAR) T programme, DSG3-CAART (targeting DSG3), and puts in place a seven-year Supply Agreement. The financial arrangements of this LSA are in line with comparable deals the Group has previously secured.

Cabaletta Bio's DSG3-CAART product candidate utilises Cabaletta's CAAR T approach, in which the patient's own T cells are genetically engineered to express the target autoantigen and direct them to recognise and eliminate the pathogenic B cells. DSG3-CAART is being evaluated in the DesCAARTes™ Phase 1 clinical trial as a potential treatment for patients with mucosal pemphigus vulgaris (mPV), a prototypical B cell-mediated autoimmune disease. The LSA also allows for the parties to initiate additional projects in the future.

John Dawson, Chief Executive Officer of Oxford Biomedica, said: *"Cabaletta Bio is one of the leading companies developing engineered T cells designed to treat patients with autoimmune diseases. We are delighted to announce this new collaboration which strengthens our portfolio of relationships with leaders in the gene-modified cell therapy field.*"

Gwendolyn Binder, Ph.D., EVP of Science and Technology, Cabaletta Bio, said: *"Oxford Biomedica's LentiVector® platform technology is well established with regulators, and we are impressed by their continuous process improvements, GMP manufacturing and validation expertise. We are very pleased to be working with them to support the clinical and commercial development of our DSG3-CAART program."*

-Ends-

Enquiries:

Oxford Biomedica plc: T: +44 (0)1865 783 000 / E: ir@oxb.com

John Dawson, Chief Executive Officer
Stuart Paynter, Chief Financial Officer
Sophia Bolhassan, Head of Investor Relations

Consilium Strategic Communications: T: +44 (0)20 3709 5700

Mary-Jane Elliott / Matthew Neal

About Oxford Biomedica
Oxford Biomedica (LSE:OXB) is a leading, fully integrated, gene and cell therapy group focused on developing life changing treatments for serious diseases. Oxford Biomedica and its subsidiaries (the "Group") have built a sector leading lentiviral vector delivery platform (LentiVector®), which the Group leverages to develop in vivo and ex vivo products both inhouse and with partners. The Group has created a valuable proprietary portfolio of gene and cell therapy product candidates in the areas of oncology, CNS disorders and liver diseases. The Group has also entered into a number of partnerships, including with Novartis, Bristol Myers Squibb, Sio Gene Therapies, Orchard Therapeutics, Santen, Beam Therapeutics, Boehringer Ingelheim and Arcellx, through which it has long-term economic interests in other potential gene and cell therapy products. Additionally, the Group has signed a 3-year master supply and development agreement with AstraZeneca for large-scale manufacturing of the adenoviral based COVID-19 vaccine candidate, AZD1222. Oxford Biomedica is based across several locations in Oxfordshire, UK and employs more than 740 people. Further information is available at www.oxb.com

SCHEDULE 5

OXB Patent Rights [***]

SCHEDULE 6

Third Party Cell Lines and Other Physical Materials

[***]

SCHEDULE 7

Quality Agreement

[***]

SCHEDULE 8

[***]

[***]

Oxford Biomedica (UK) Ltd
Windrush Court, Transport Way, Oxford 0X4 6LT, United Kingdom
Telephone: +44 (0) 1865 783 000, www.oxb.com
Registered in England and Wales with registration number 3028927

Exhibit 21.1

List of Subsidiaries

None.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-234367) pertaining to the Cabaletta Bio, Inc. 2018 Stock Option and Incentive Plan, the Cabaletta Bio, Inc. 2019 Stock Option and Incentive Plan, and the Cabaletta Bio, Inc. 2019 Employee Stock Purchase Plan,
(2) Registration Statement (Form S-8 No. 333-237484) pertaining to the Cabaletta Bio, Inc. 2019 Stock Option and Incentive Plan and the Cabaletta Bio, Inc. 2019 Employee Stock Purchase Plan,
(3) Registration Statement (Form S-3 No. 333-250006) of Cabaletta Bio, Inc., and
(4) Registration Statement (Form S-8 No. 333-254342) pertaining to the Cabaletta Bio, Inc. 2019 Stock Option and Incentive Plan and the Cabaletta Bio, Inc. 2019 Employee Stock Purchase Plan

of our report dated March 17, 2022, with respect to the financial statements of Cabaletta Bio, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania

March 17, 2022

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Steven Nichtberger, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2021 of Cabaletta Bio, Inc. (the "registrant");

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 17, 2022

By: /s/ Steven Nichtberger

Steven Nichtberger, M.D.
Chief Executive Officer and President
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Anup Marda, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2021 of Cabaletta Bio, Inc. (the "registrant");

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 17, 2022

By: /s/ Anup Marda

Anup Marda
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

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 of Cabaletta Bio, Inc. (the "Company") on Form 10-K for the fiscal year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 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 result of operations of the Company.

Date: March 17, 2022

By: /s/ Steven Nichtberger

Steven Nichtberger, M.D.
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

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 of Cabaletta Bio, Inc. (the "Company") on Form 10-K for the fiscal year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 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 result of operations of the Company.

Date: March 17, 2022

By: /s/ Anup Marda

Anup Marda
Chief Financial Officer
(Principal Accounting and Financial Officer)