0-K?

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-K

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

For the fiscal year ended December 31, 2020

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 001-38811

TCR2 Therapeutics Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**47-4152751**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)

100 Binney Street, Suite 710
Cambridge, Massachusetts 02142
(Address of Principal Executive Offices)

(617) 949-5200
(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 Par Value	TCRR	The Nasdaq Stock Market, LLC

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 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 ☒

Aggregate market value of the voting stock held by non-affiliates of the registrant as of June 30, 2020: $216,090,573

As of March 1, 2021, there were 38,137,440 shares of the registrant's Common Stock, $0.0001 par value per share, outstanding.

TCR2 Therapeutics Inc.

Table of Contents

SUMMARY OF THE MATERIAL AND OTHER RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous material and other risks and uncertainties that you should be aware of in evaluating our business. These risks are described more fully in "Item 1A—Risk Factors," and include, but are not limited to, the following:

- Our approach to the discovery and development of product candidates based on our TRuC-T cell platform represents a novel approach to cancer treatment, which creates significant challenges for us. Further, we are very early in our development efforts. Most of our product candidates are still in preclinical development. 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.
- Our business is highly dependent on our clinical trials for our lead product candidates, gavo-cel and TC-110, and we must complete IND-enabling studies and clinical testing before we can seek regulatory approval and begin commercialization of any of our product candidates. We cannot be certain that we will be able to complete ongoing clinical trials, initiate future planned clinical trials, or advance our product candidates into additional trials, or to successfully develop, or obtain regulatory approval for, or successfully commercialize, any of our product candidates.
- We have limited experience as a company in conducting clinical trials. Clinical development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future clinical trial results. If our preclinical studies and clinical trials are not sufficient to support regulatory approval of any of our product candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such product candidate.
- Manufacturing and administering our product candidates are complex and 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 TRuC-T cells for clinical trials or for commercial purposes could be delayed or stopped. We plan to 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 and the use of third-party manufacturing suites, which will be costly, time-consuming, and which may not be successful.
- The market opportunities for our product candidates may be relatively small as it will be limited to those patients who are ineligible for or have failed prior treatments and our estimates of the prevalence of our target patient populations may be inaccurate.
- We plan to rely on third parties to conduct our clinical trials. If these third parties do not properly and 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. If these third parties do not properly and 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.
- 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. We have incurred significant losses since inception, and we expect to incur losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future.
- The current outbreak of novel coronavirus, or COVID-19, has caused, and could continue to cause, severe disruptions in the U.S., regional and global economies. COVID-19 has affected our on-going clinical trials and could seriously harm our development efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.
- If we are unable to obtain and maintain patent protection for any products we develop and for our technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop, and our technology may be adversely affected.
- 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.
- 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.
- 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 stock price has been and will likely continue to be volatile. Securities class action or other litigation involving our company or members of our management team could also substantially harm our business, financial condition and results of operations.
- We are an emerging growth company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors. We are also a "smaller reporting company," and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K of TCR2 Therapeutics Inc. (the "Company") contains or incorporates statements that constitute forward-looking statements within the meaning of the federal securities laws. Any statements that do not relate to historical or current facts or matters are forward looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "could", "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "projects", "potential," "continue" or the negative of these terms or other comparable terminology. Forward-looking statements appear in a number of places in this Annual Report on Form 10-K and include, but are not limited to, statements about:

- the timing of preclinical studies and clinical trials of gavo-cel, TC-110 and any other product candidates;
- our need to raise additional funding before we can expect to generate any revenues from product sales;
- our ability to submit our planned INDs, conduct successful clinical trials and obtain regulatory approval for gavo-cel, TC-110 or any other product candidates that we may identify or develop;
- the ability of our TRuC-T cell platform to generate and advance additional product candidates;
- our ability to establish an adequate safety, potency and purity profile for gavo-cel, TC-110 or any other product candidates that we may pursue;
- our ability to manufacture gavo-cel, TC-110 or any other product candidate in conformity with our specifications and with the U.S. Food and Drug Administration's requirements and to scale up manufacturing of our product candidates to commercial scale, if approved;
- the implementation of our strategic plans for our business, any product candidates we may develop and our technology;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- the rate and degree of market acceptance and clinical utility for any product candidates we may develop;
- our expectations related to the use of proceeds from our initial public offering;
- our estimates regarding our expenses, future revenues, capital requirements and our needs for additional financing;
- our ability to maintain and establish collaborations;
- our ability to effectively manage our anticipated growth;
- developments relating to our competitors and our industry, including the impact of government regulation;
- our estimates regarding the market opportunities for our product candidates;
- the impact of the ongoing COVID-19 pandemic on our business, operations, strategy, goals and anticipated timelines;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals; and
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act, or the JOBS Act;
- our financial performance; and
- other risks and uncertainties, including those listed under the section titled "Risk Factors."

Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. You are urged to carefully review the disclosures we make concerning these risks and other factors that may affect our business and operating results under "Item 1A. Risk Factors" in this Annual Report on Form 10-K. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this document. The Company does not intend, and undertakes no obligation, to update any forward-looking information to reflect events or circumstances after the date of this document or to reflect the occurrence of unanticipated events, unless required by law to do so.

Part I

Except where the context otherwise requires or where otherwise indicated, the terms "TCR^2," "TCRR," "we," "us," "our," "our company," "the company," and "our business" refer to TCR^2 Therapeutics Inc. and its consolidated subsidiaries.

Item 1. Business

Overview

We are a clinical-stage cell therapy company developing a pipeline of novel T cell therapies for patients suffering from cancer by powering the T cell receptor (TCR) with our proprietary, first-in-class TCR Fusion Construct T cells (TRuC-T cells). Designed to overcome the limitations of current cell therapy modalities, our TRuC-T cells specifically recognize and kill cancer cells by harnessing the entire TCR signaling complex, which we believe is essential for T cell therapies to be effective in patients with solid tumors.

Our lead TRuC-T cell targeting solid tumors is gavocabtagene autoleucel (gavo-cel, formerly TC-210). We are conducting our Phase 1/2 clinical trial for gavo-cel to treat patients with non-small cell lung cancer (NSCLC), ovarian cancer, malignant pleural/peritoneal mesothelioma and cholangiocarcinoma. We estimate the patient population for gavo-cel in the four indications which we are exploring in our clinical trial is up to 80,000 patients in the United States alone. Based on interim data readouts from patients in dose escalation in our Phase 1/2 clinical trial, gavo-cel has demonstrated consistent clinical benefit, with every patient experiencing tumor regression and a 100% disease control rate (DCR). As of the November 24, 2020 cutoff date, we have observed a 38% Overall Response Rate (ORR) with three RECIST partial responses (PRs) (2 confirmed and 1 unconfirmed PRs), including the first ovarian cancer patient to ever achieve a PR with an engineered cell therapy and one mesothelioma patient achieving a complete metabolic response. The safety profile of gavo-cel continues to be manageable with no neurotoxicity or on-target, off-tumor toxicities observed. Based on our mesothelin cutoff screening protocol (confirmed positive mesothelin expression on ≥50% of tumor cells that are 2+ and/or 3+ by immunohistochemistry), 45% of patients screened have been eligible to be enrolled in our clinical trial. We have received an Food and Drug Administration (FDA) Orphan Drug Designation for the treatment of mesothelioma with gavo-cel and also plan to apply for FDA Fast Track designation for gavo-cel. We anticipate interim updates of the Phase 1 portion of the gavo-cel Phase 1/2 clinical trial throughout 2021.

Our lead TRuC-T cell targeting hematological malignancies is TC-110. In the Phase 1/2 clinical trial for TC-110, we are treating patients with adult acute lymphoblastic leukemia (aALL) and with aggressive or indolent non-Hodgkin's lymphoma (NHL). We estimate the patient population for TC-110 in the three indications which we are exploring in our clinical trial is up to 13,700 patients in the United States alone. In our preclinical studies of TC-110, we have observed better anti-tumor activity, improved persistence and lower cytokine release compared to chimeric antigen receptor (CAR) T cells we engineered to target CD19. Based on these preclinical studies, we believe we can improve on the efficacy and safety of current CD19 therapies. We continue to treat patients in the dose escalation portion of the study and anticipate an interim update from the Phase 1 portion of the TC-110 Phase 1/2 clinical trial in 2021.

In addition to our two lead clinical programs, we are expanding our pipeline by utilizing our versatile platform to address some of the primary challenges to cell therapies such as the hostile and immunosuppressive tumor microenvironment. These include enhancements, such as: TC-510, our TRuC-T cell co-expressing a PD-1:CD28 switch receptor that converts inhibitory PD-1 signaling into positive costimulation and IL-15 pathway enhancements to improve T cell persistence; dual targeting TRuC-T cells to combat tumor heterogeneity; and other accessories to combat the tumor microenvironment. We are also pursuing new targets such as CD70 and GPC3 for which we believe TRuC-T cells offer advantages over existing therapeutic modalities. We continue to advance our allogeneic, or off-the-shelf, TRuC-T cell approaches to simplify manufacturing, reduce cost of therapy, and improve patient access. We anticipate filing an IND for TC-510 in 2021, presenting preclinical data for our autologous CD70 and allogeneic mesothelin TRuC-T cell programs, among others, throughout 2021; and selecting a development candidate for our allogeneic program in 2021.

Our TRuC platform originated from the work of our scientific founder, Dr. Patrick Baeuerle, a leading immunologist who developed the world's first bispecific antibody, Blincyto®. We have assembled a scientific team with deep translational medicine, manufacturing, and immunotherapy expertise to develop optimally designed TRuC-T cells to treat patients suffering from a wide range of hematologic cancers and solid tumors. Our management team brings extensive experience in cell therapy, including CAR-T and TCR-T cells, and all phases of drug discovery, development and manufacturing gained at large pharmaceutical and biotechnology companies, and we believe they will enable us to continue advancing our pipeline and expanding the capabilities of our platform.

Our Strategy

Our goal is to cure certain cancers with our TRuC-T cell therapies. We intend to make a difference in the lives of patients by building a fully integrated cancer cell therapy company offering the first HLA-independent T cell therapy that works through activation of the full TCR. The key components of our strategy are:

- *Rapidly advance clinical development of our lead solid tumor program and lead hematological malignancy program to validate our TRuC platform.* Our strategy for our TRuC platform includes the initial pursuit of validated immunotherapy targets, such as mesothelin and CD19, based on well-characterized disease models in an attempt to minimize target risk. We are treating patients with gavo-cel, our lead TRuC-T cell targeting mesothelin-expressing solid tumors, in the dose escalation portion of our Phase 1/2 clinical trial. We are treating patients with TC-110, our lead TRuC-T cell targeting patients with CD19-positive B-cell hematological malignancies, in the dose escalation portion of our Phase 1/2. We believe promising clinical trial results in these initial programs could translate into broader therapeutic potential for our TRuC platform.

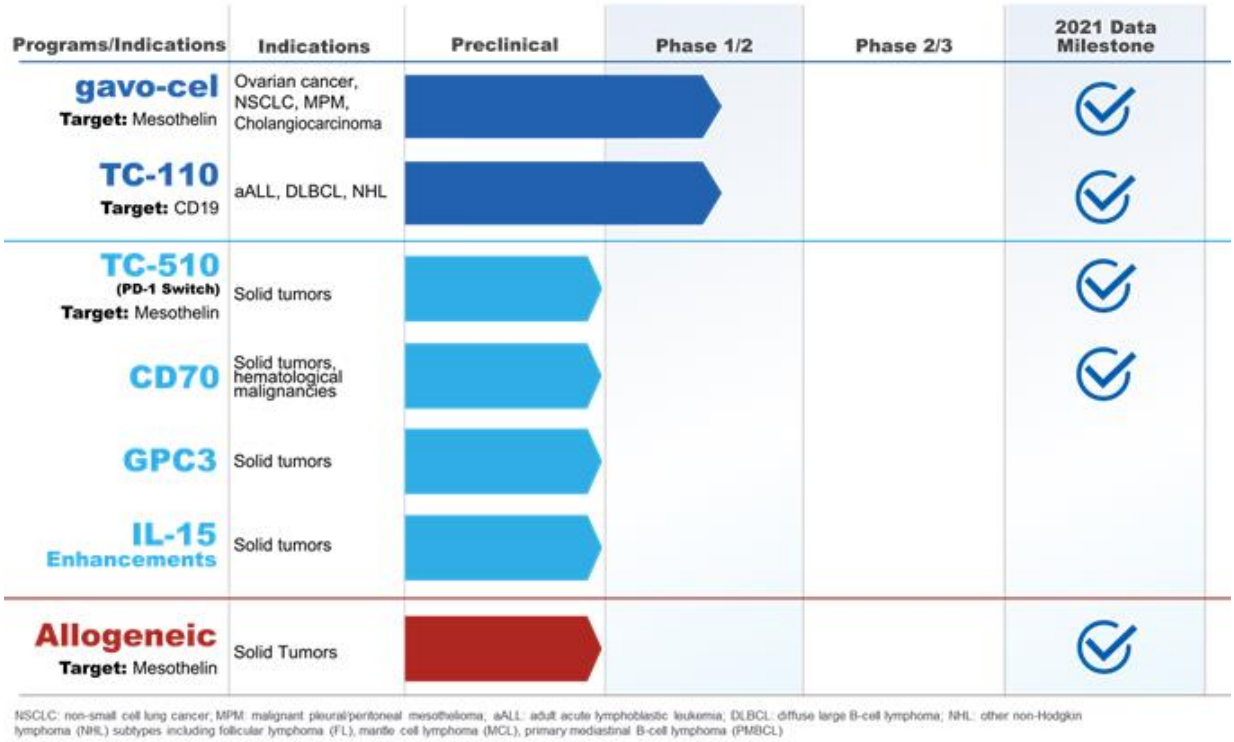
- *Exploit the versatility of our platform to broaden our pipeline.* We are exploring new targets such as CD70 and GPC3 for which we believe TRuC-T cells offer advantages to existing therapeutic modalities and are developing several additional enhancements such as the PD-1:CD28 switch receptor that may be incorporated into our future product candidates to overcome tumor defense mechanisms, including dual-antigen targeting TRuC-T cells to minimize the possibility of antigen escape and cancer relapse. We are also developing several strategies to counter the prominent immunosuppressive mechanisms in the tumor microenvironment, including interference with immune checkpoint pathways. Further, we are evaluating proprietary designs for allogeneic, or off-the-shelf, TRuC-T cells which will enable us to broaden access to patients.

- *Scale our manufacturing capacity to match our future product needs.* We plan to develop our own manufacturing capabilities. We are currently manufacturing GMP-grade clinical lots for gavo-cel through third-party contractors. We have also established a manufacturing presence in both the US and UK by entering into agreements with ElevateBio BaseCamp and Cell Therapy Catapult Limited (Catapult). Our agreement with ElevateBio will support the manufacturing demand for the expansion portion of the gavo-cel Phase 1/2 clinical trial and enables utilization of our own equipment in close proximity to our U.S. headquarters in Cambridge, MA. The Catapult agreement will allow us to manufacture our TRuC-T cells using our own personnel at Catapult's facility while expanding our capacity to supply future clinical trials. We can also apply our learnings from ElevateBio and Catapult towards our own future commercial manufacturing and multiple suppliers will diversify and help to solidify our clinical trial manufacturing capacity. If our clinical trials are successful, given the size of the patient population that can potentially be targeted by our product candidates, we plan to build our own manufacturing facility.

- *Retain significant economic and commercial rights to our product candidates and potentially acquire or in-license strategic complementary businesses, assets or technologies.* We currently own all rights to our product candidates and programs and intend to build a fully integrated cell therapy company. We intend to maintain product rights in key geographies, in particular for gavo-cel. We believe the versatility of our platform presents an opportunity for us to selectively form strategic collaborations and acquire or in-license complementary businesses, assets or technologies allowing us to expand our capabilities and product offerings into other therapeutic areas and potentially accelerate the development and maximize the commercial potential of our product candidates.

Our Pipeline

The versatility of our platform is highlighted by our lead programs and multiple approaches in development. We have generated a broad pipeline with assets that address both solid tumors and hematological malignancies. Our product candidates are listed in the figure below.



NSCLC: non-small cell lung cancer; MPM: malignant pleural/peritoneal mesothelioma; aALL: adult acute lymphoblastic leukemia; DLBCL: diffuse large B-cell lymphoma; NHL: other non-Hodgkin lymphoma (NHL) subtypes including follicular lymphoma (FL), mantle cell lymphoma (MCL), primary mediastinal B-cell lymphoma (PMBCL)

Our Focus

According to a 2017 press release from the FDA upon the licensure of the first engineered T cell therapy for cancer, the field is "entering a new frontier in medical innovation with the ability to reprogram a patient's own cells to attack a deadly cancer." We founded our company to build on these early T cell therapy innovations while addressing their limitations and making our product candidates available to a broader patient population.

The immune system is responsible for protecting the human body against viral and bacterial infections, as well as mutated and cancerous cells. A critical component of the immune system are T cells that are able to target and kill these agents by using TCR recognition of cell surface markers known as antigens. Existing T cell therapies for cancer, including CAR-T cells and engineered TCR-T cells, attempt to replicate this mechanism. While current T cell therapies have shown encouraging efficacy data, they have limitations that we believe our TRuC-T cell product candidates can address by leveraging the entire TCR complex.

Our Approach Utilizes the Full T-Cell Receptor

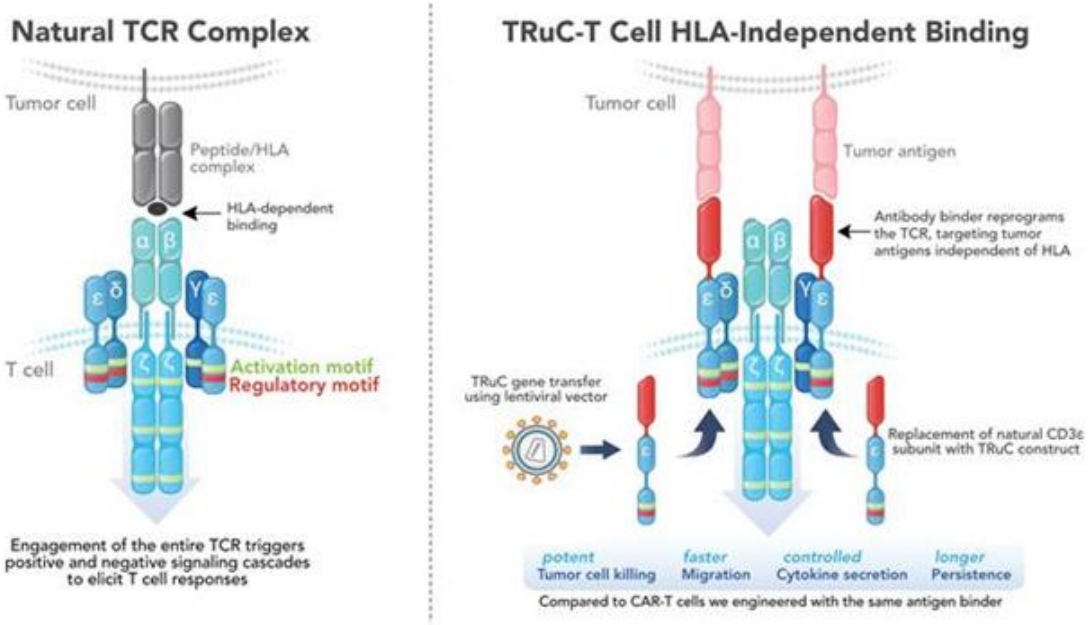
The TCR is one of the body's most complex receptors, composed of an antigen-recognizing heterodimer (TCRα and TCRβ chains) which binds to specific peptide-MHC ligands in association with a complex of signaling subunits, collectively called CD3: CD3γ, CD3δ, and two subunits each of CD3ε and CD3ζ. The contribution and interplay of the TCR's six different receptor subunits to its very broad and complex signaling activities in T cells is not fully understood but we believe all subunits play an important role in regulating and tuning activation signals downstream of the TCR. In total, the six different CD3 subunits contain ten immune receptor tyrosine-based activation motifs (ITAM) and the multiplicity of ITAMs within the TCR regulates the signaling potency and thereby the strength of T cell activation following TCR ligation. Besides ITAMs, other unique motifs in the intracellular domains of CD3γ, CD3δ, CD3ε, and CD3ζ are crucial for homeostasis, negative feedback regulation, signaling, and function of the TCR complex. In contrast to CAR-Ts, which operate as stand-alone receptors utilizing only one of the six TCR subunits (CD3ζ), TRuCs fully integrate into the TCR complex and therefore have the potential utilize the full signaling capacity of the TCR and take advantage of its intrinsic regulatory mechanisms.

Our Novel T-Cell Receptor Fusion Construct (TRuC) Platform

We are pioneering the development of a novel, transformative T cell engineering platform which, based on its design and our preclinical studies, we believe has the potential to address the shortcomings of CAR-T cells and TCR-T cells and is fundamentally different from these existing approaches. Research over more than two decades has shown that each of the TCR subunits makes distinct contributions to the activation and regulation of T cells and the sum of the TCR subunits is required to optimally activate and control the function of T cells. We believe that engaging the entire TCR signaling complex is required to fully realize the potential of T cells in their fight against cancer.

Our T cell engineering approach relies upon natural TCR elements to produce therapeutic T cells that function independently of HLA restriction. To that end, we fuse a cancer antigen recognition domain (i.e. antibody-based binder) directly to a subunit of the TCR and use a lentiviral vector to transfer the genetic information for the TRuC construct into a patient's own T cells. This modified subunit then naturally integrates into the native TCR complex, creating an engineered T cell equipped with a new "homing device" to detect and engage a specific antigen on the surface of cancer cells. Upon antigen engagement, these T cells harness the entire TCR to produce a highly potent T cell response against cancer. We refer to T cells engineered with our TCR fusion constructs as TRuC-T cells. In preclinical studies of both solid tumors and hematological malignancies we have observed greater anti-tumor activity, longer persistence and less cytokine release compared to CAR-T cells we have engineered to target the same cancer antigen. Our findings suggest that the signal delivered through the full TCR by TRuCs results in efficient T cell activation while avoiding overactivation and overproduction of cytokines as occurs in CARs. We believe that these properties could translate into more durable responses with potentially fewer adverse events for patients with cancer.

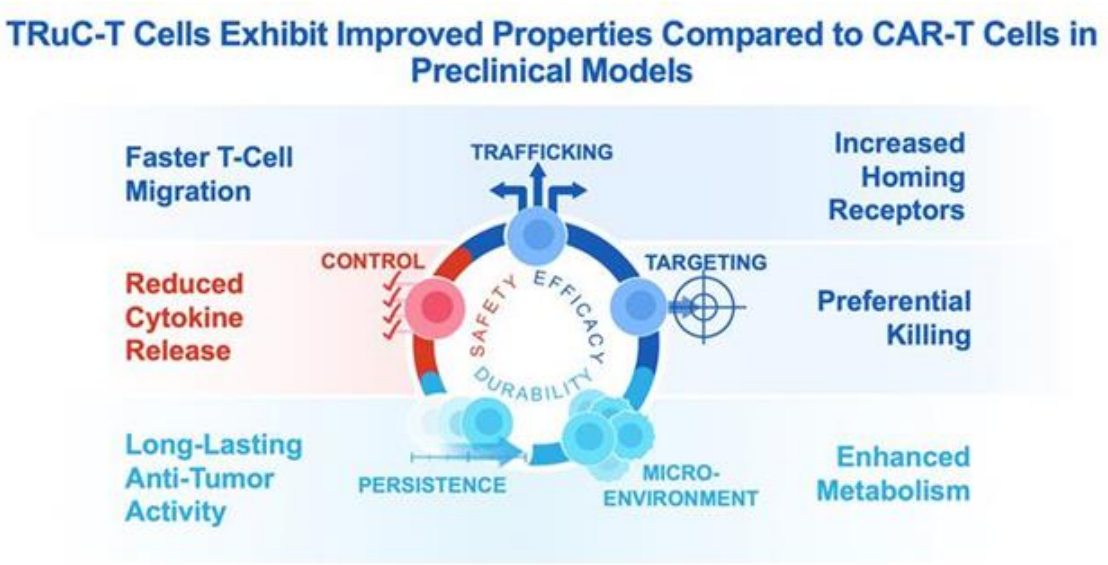
The figure below describes the natural HLA-restricted TCR complex as compared to the HLA-independent TRuC TCR.



Our platform enables the design of TRuC-T cells with a number of potential advantages, as described in the table below:

ATTRIBUTES	FEATURES	MECHANISMS	DESIRED PATIENT OUTCOME
Optimized Signaling	TRuC construct integrates into and utilizes the full signaling capacity of the natural TCR	• Naturally controlled T cell responses through TCR regulatory motifs • Avoids cytokine overproduction • No requirement for built-in costimulatory domain	• Produce a more powerful, well-controlled anti-tumor T cell response • Lower risk of adverse events
Solid Tumor Efficacy	Potent elimination of solid tumors with long-term functional persistence	• Efficient solid tumor penetration and retention • Favorable metabolic profile promotes T cell fitness • Promotion of memory T cell phenotype	• Overcomes restricted T cell migration in solid tumors • Long-term persistence to achieve durable responses
Versatile Targeting	Reprogramming of the TCR by antibody-based binder recognition of tumor antigens	• HLA-independent tumor antigen recognition through the full TCR	• Avoids HLA downregulation as a mechanism of escape/relapse
		• Ability to attack tumors based on the recognition of two different antigens	• Improved response rates in tumors with heterogeneous target antigen expression
	Dual targeting	• Screening of diverse binder pools yields TRuC-T cells with optimal properties	• Reduced risk of relapse due to antigen escape
	Broad range of available binder formats allows identification of optimized TRuC for each target	• Binder formats include, but are not limited to, single-chain variable fragments, single-domain antibodies and receptors	• TRuC optimization leads to increased likelihood of clinical activity

Our goal is to improve upon the efficacy and safety of T-cell therapies by enhancing trafficking of T cells into tumors, tumor antigen targeting, the ability to withstand the tumor microenvironment, long-lasting T-cell persistence, and a controlled anti-tumor response. In our preclinical studies, TRuC-T cells have shown improvements in each of these key characteristics compared to CAR-T cells we have engineered with the same binders.



We use our TRuC-T cell platform to target many different cancer antigens. Our core format, in which we target a single cancer antigen, is known as a mono TRuC-T cell. Our mono TRuC-T cell product candidates have shown promising anti-tumor activity and persistence in our preclinical studies.

We are expanding our core format with a series of next-generation enhancements that may further improve clinical outcomes. These fall into four broad categories:

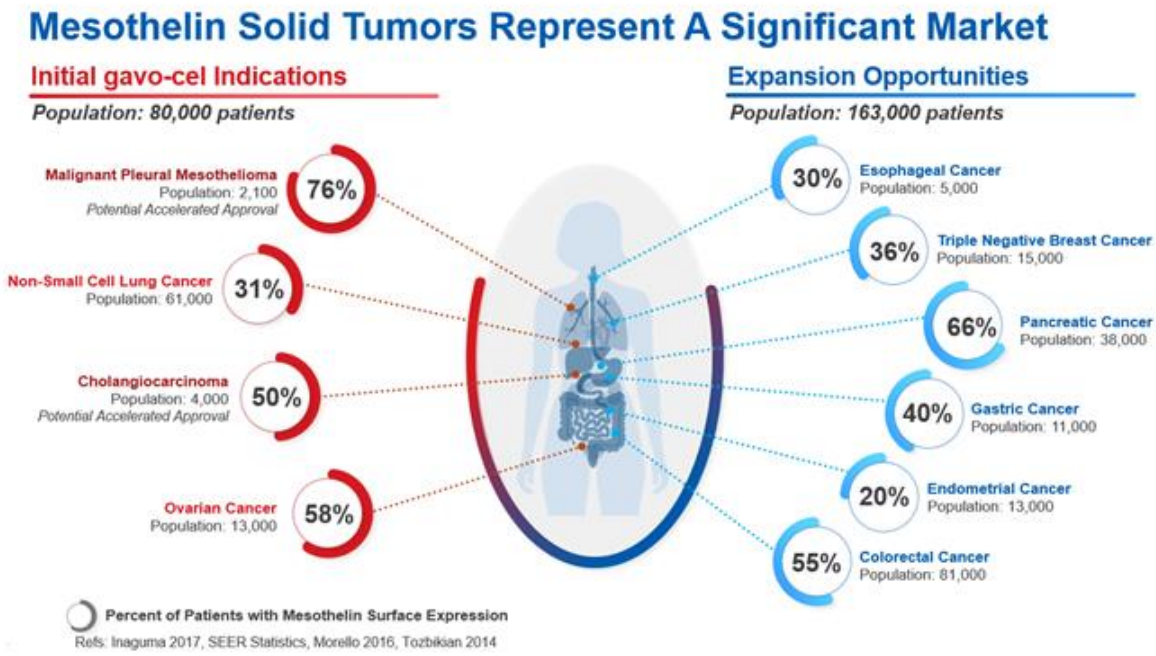
- First, we are developing formats that target two antigens, known as dual TRuC-T cells, which could improve tumor response in patients who express more than one cancer antigen and combat potential antigen escape, which is a leading mechanism of cancer relapse in patients receiving CAR-T cell therapy.
- Second, we are developing several strategies to counter the immunosuppressive microenvironment of solid tumors including mechanisms to block a key cancer defense known as the PD-1 pathway, which can inhibit anti-tumor responses by T cells.
- Third, we are evaluating proprietary designs for allogeneic or off-the-shelf TRuC-T cells, aiming to give patients faster access to and reduce the costs of TRuC-T cell therapies.

- Finally, due to the TRuC platform's versatility, we have the capability to target many different cancer antigens and we are focused on the discovery and validation of novel targets to broaden the reach of TRuC-T cells.

gavo-cel: Our Lead Mono TRuC-T Cells Targeting Mesothelin Positive Solid Tumors

Our most advanced TRuC-T cell product candidate is gavo-cel, which targets mesothelin-positive solid tumors. Mesothelin is a cell-surface protein whose expression is mostly restricted to mesothelial cell layers lining the pleura, pericardium and peritoneum but which is not known to be expressed on any vital organs. While its expression on normal tissues is low, mesothelin is highly expressed in many solid tumors. The cancer types that we intend to treat in our Phase 1/2 clinical trial include non-small cell lung cancer, ovarian cancer, malignant pleural/peritoneal mesothelioma and cholangiocarcinoma. These cancers represent a patient population of up to 80,000 in the United States alone. By comparison, the addressable U.S. patient population with hematological malignancies for approved CD19-directed CAR-T therapies is estimated to be approximately 8,000. Additionally, we estimate potential expansion opportunities in six additional indications that overexpress mesothelin to represent a population of up to 163,000 patients.

In dose escalation in our Phase 1/2 clinical trial, gavo-cel has demonstrated consistent clinical benefit, with every patient experiencing tumor regression and a 100% DCR. We have observed a 38% ORR with three RECIST PRs, two mesothelioma patients and the first ovarian cancer patient to ever achieve a PR with an engineered cell therapy. We have received an FDA Orphan Drug Designation for the treatment of mesothelioma with gavo-cel and also plan to apply for FDA Fast Track designation for gavo-cel. We anticipate interim updates of the Phase 1 portion of the gavo-cel Phase 1/2 clinical trial throughout 2021.



Mesothelin is overexpressed on the cell surface in multiple cancers, including approximately 76% of malignant pleural mesotheliomas (the most common type of mesothelioma), 58% of ovarian cancers and 31% of NSCLC, among others. The following figure illustrates the proportion of cancer patients with mesothelin expressed on the surface of their tumors and are therefore potential candidates for gavo-cel therapy.

NSCLC Background

NSCLC remains the leading cause of cancer-related mortality worldwide, accounting for approximately 18% of all cancer deaths. There are an estimated 194,000 new cases in the United States annually with an estimated 61,000 (31%) expressing mesothelin on the cell surface.

Patients with metastatic NSCLC have a poor prognosis with a median survival of approximately ten months and a five-year survival rate of approximately 15% to 20%. While recent advances with checkpoint inhibitors have demonstrated promising results, the majority of patients treated with these agents do not derive a long-term benefit. Notably, no standard of care is available for patients failing to respond or relapsing after checkpoint inhibitor therapy, a segment of the NSCLC market which is expected to grow in size as the use of immune checkpoint inhibitors increases in first- and second-line settings.

Ovarian Cancer Background

Epithelial ovarian cancer comprises approximately 90% of all ovarian malignancies. Approximately 22,000 patients in the United States were diagnosed with ovarian cancers in 2020 with an estimated 13,000 cases expressing mesothelin on the cell surface.

Taxane and platinum-based combinations have been the backbone of ovarian cancer treatment for the past 20 years, despite having very low efficacy rates (below 15%) in patients with advanced forms of the disease. The majority of patients progressing after platinum retreatment have no approved treatment options. Relapsed, recurrent ovarian cancer remains incurable with an estimated 14,000 deaths from ovarian cancer in 2020 in the United States alone.

Malignant Pleural/Peritoneal Mesothelioma Background

Malignant mesothelioma is a rare and aggressive malignancy arising from mesothelial cells lining the cavity surrounding the lungs (pleura), abdomen (peritoneum), heart (pericardium) or testes. Patients with either malignant pleural mesothelioma or malignant peritoneal mesothelioma are eligible for enrollment in our Phase 1/2 clinical trial of gavo-cel.

Malignant pleural mesothelioma is the most common form of mesothelioma, accounting for an estimated 84% of cases. Asbestos exposure causes approximately 80% of malignant pleural mesothelioma cases. There are an estimated 2,700 new cases per year of malignant mesothelioma in the United States of which an estimated 2,100 express mesothelin on the cell surface.

Effective treatment options for patients with malignant pleural mesothelioma are very limited. In October 2020, the FDA approved Opdivo (nivolumab) in combination with Yervoy (ipilimumab) for the first-line treatment of adults with malignant pleural mesothelioma that cannot be removed by surgery. This is the first drug regimen approved for mesothelioma in 16 years and the second FDA-approved systemic therapy for mesothelioma. In second line, the standard of care recommended is chemotherapy that includes a platinum salt and an anti-folate. Unfortunately, the ORR is 17% to 40% and the median overall survival of patients with malignant pleural mesothelioma is 12 to 19 months when systemic chemotherapy is used with or without anti-angiogenic agents or targeted therapy. Malignant mesothelioma causes approximately 2,500 deaths in the United States annually.

Malignant peritoneal mesothelioma is the second-most common form of mesothelioma, accounting for an estimated 10% of cases. While malignant peritoneal mesothelioma is less commonly studied than malignant pleural mesothelioma, similar systemic chemotherapy regimens of platinum and antifolate combinations are often used. The prognosis for patients with malignant peritoneal mesothelioma is poor as only 35% of patients survive more than two years after diagnosis.

Cholangiocarcinoma Background

Cholangiocarcinoma is a form of cancer that is composed of mutated epithelial cells that originate in the bile ducts. There are an estimated 8,000 new cholangiocarcinoma cases in the United States per year with about 50% expressing mesothelin on the cell surface. Most patients with cholangiocarcinoma have advanced-stage disease at presentation, for which the available standard-of-care chemotherapy (gemcitabine and cisplatin) renders a median overall survival of less than one year. Multiple products, including checkpoint inhibitors and others, are being tested in clinical trials, but cholangiocarcinoma remains an unmet medical need. Cholangiocarcinoma causes over 7,000 deaths per year in the United States alone.

We plan to submit an FDA Orphan Drug Designation application for gavo-cel's treatment of cholangiocarcinoma. In addition, we plan to apply for FDA Fast Track, FDA Breakthrough Therapy and additional Orphan Drug Designations, as well as Accelerated Approvals, where applicable.

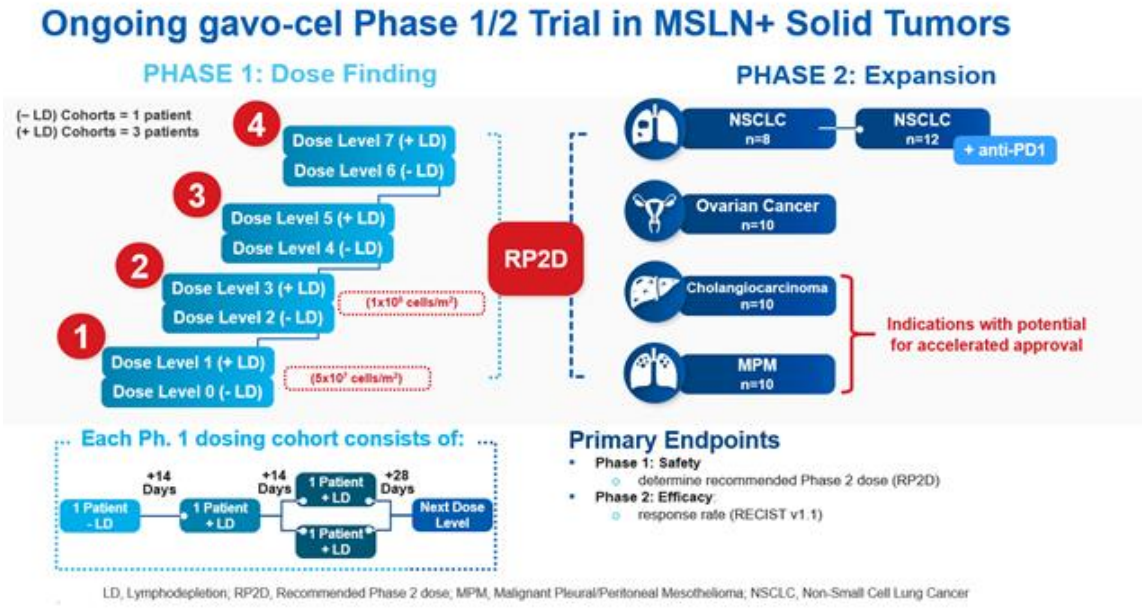
gavo-cel Phase 1/2 Trial in Mesothelin-Positive Tumors

We have initiated a Phase 1/2 clinical trial of gavo-cel in patients with mesothelin-positive NSCLC, ovarian cancer, malignant pleural/peritoneal mesothelioma and cholangiocarcinoma. Given the high unmet need and limited treatment options in malignant pleural/peritoneal mesothelioma and cholangiocarcinoma, our goal is to obtain Fast Track designations for gavo-cel in those indications from the FDA, which we believe will provide the potential for accelerated licensing based on Phase 2 clinical trial data.

Our Phase 1/2 clinical trial consists of two parts:

- In the Phase 1 portion of the clinical trial, patients will receive gavo-cel at four dose levels with or without lymphodepleting chemotherapy to determine the recommended Phase 2 dose (RP2D). At each dose level, gavo-cel T cells will be first given without lymphodepletion to one patient and, if deemed safe, given to the subsequent three patients following lymphodepleting chemotherapy.

- The objective of the Phase 2 portion of the clinical trial, in addition to further characterizing the safety profile of gavo-cel, is to evaluate the efficacy of gavo-cel in mesothelin-expressing cancers as assessed by overall response rate (ORR) according to standard Response Evaluation Criteria In Solid Tumors (RECIST) v1.1 criteria (ORR: complete response + partial response). Secondary endpoints will include time to response, duration of response, progression free survival and overall survival. Approximately 50 patients will receive gavo-cel at the RP2D schedule and will be stratified according to their cancer diagnosis in four groups: NSCLC, ovarian cancer, malignant pleural/peritoneal mesothelioma and cholangiocarcinoma. A total of ten patients per indication will be infused with gavo-cel T cells, except in the NSCLC cohort where 20 patients will be treated, including eight receiving gavo-cel as single agent and 12 receiving gavo-cel in combination with the PD-1 blocking antibody.



Clinical findings

On December 13, 2020, we announced positive interim data from the ongoing Phase 1 portion of the gavo-cel Phase 1/2 clinical trial for mesothelin-expressing solid tumors. As of the November 24, 2020 data cutoff, three PRs according to RECIST 1.1 criteria have been recorded among the first eight patients treated on study in dose escalation, with our first ovarian cancer patient having achieved a confirmed PR in target lesions and a complete response in a non-target lesion through month six. This patient developed new lesions beginning after month three and is rated by RECIST as having progressive disease beginning with month four. In addition, the first patient treated at a higher gavo-cel dose ($1x10^8/m^2$) without lymphodepletion achieved stable disease through two months without any significant toxicities, which has allowed patients to start treatment at that dose with the addition of lymphodepletion. The toxicity profile remains manageable with only two patients to date exhibiting gavo-cel-related non-hematologic grade >2 toxicity and no evidence of neurotoxicity or on-target, off-tumor toxicity. Translational data further demonstrated TRuC-T cell expansion and cytokine induction in all patients.

The primary objectives of the Phase 1 portion of the study are to define the safety profile of gavo-cel in patients whose tumors overexpress mesothelin and to determine the RP2D. Secondary objectives include ORR and DCR. Exploratory objectives include the assessment of expansion, tumor infiltration, and persistence of gavo-cel.

Summary of trial conduct, baseline characteristics and gavo-cel dose:

- **Safety Protocol:** The new clinical trial protocol amendment allows the intra-cohort safety observation periods to be reduced to 14 days from 28 days, allowing the testing of a gavo-cel dose over a minimum of 56 days compared to the previous 84 days.

- **Screening:** Forty-five percent of patients met the mesothelin expression cut-off as defined per protocol.

- **Manufacturing:** Gavo-cel products meeting protocol defined specifications have been manufactured successfully for each patient for whom apheresis material was sent into production.

- **Patient Characteristics**: Eight patients received gavo-cel including seven with mesothelioma and one with ovarian cancer with a median age of 65 years (range, 36-84 years). The median number of prior therapies was 5.5 (range, 3-9), including immune checkpoint inhibitor therapy (n=6) and anti-mesothelin therapies (n=3).

- **Gavo-cel Dose**: The eight patients disclosed to date have received gavo-cel at the following dose level (DL):

    - **DL 0:** $5x10^7$ cells/m^2 without lymphodepletion – 1 mesothelioma

    - **DL 1:** $5x10^7$ cells/m^2 following lymphodepletion – 5 mesothelioma and 1 ovarian cancer

    - **DL 2:** $1x10^8$ cells/m^2 without lymphodepletion – 1 mesothelioma

Key clinical findings from the first eight patients treated with gavo-cel:

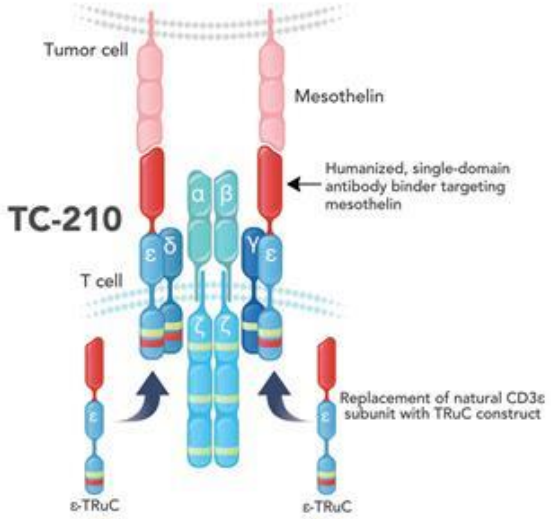
- **Safety**: Gavo-cel was generally well tolerated, with no patients experiencing neurotoxicity or on-target, off-tumor toxicities. Two (25%) patients experienced Cytokine Release Syndrome (CRS) grade 3, which was successfully managed with tocilizumab and corticosteroids.

- **Clinical Activity**: All eight patients have had at least one disease response assessment. The DCR was 100%, with all patients experiencing tumor regression. The median decrease in the sum of diameters of target lesions was 43% (range, 5% to 75%). The ORR was 38% (2 confirmed and 1 unconfirmed PRs) according to RECIST v1.1 criteria, including the first ovarian cancer patient to ever achieve a PR with an engineered cell therapy and one mesothelioma patient achieving a complete metabolic response.

- **Translational Data**: Peak gavo-cel expansion (C_{max}) occurred between days 7 and 23. C_{max} increased when gavo-cel was administered following lymphodepletion. The median peak gavo-cel expansion was 811.9 copies/µg of genomic DNA (range, 520 to 5,901 copies/µg). Cytokine induction post-gavo-cel infusion was observed in all evaluable patients, which is indicative of mesothelin target engagement.

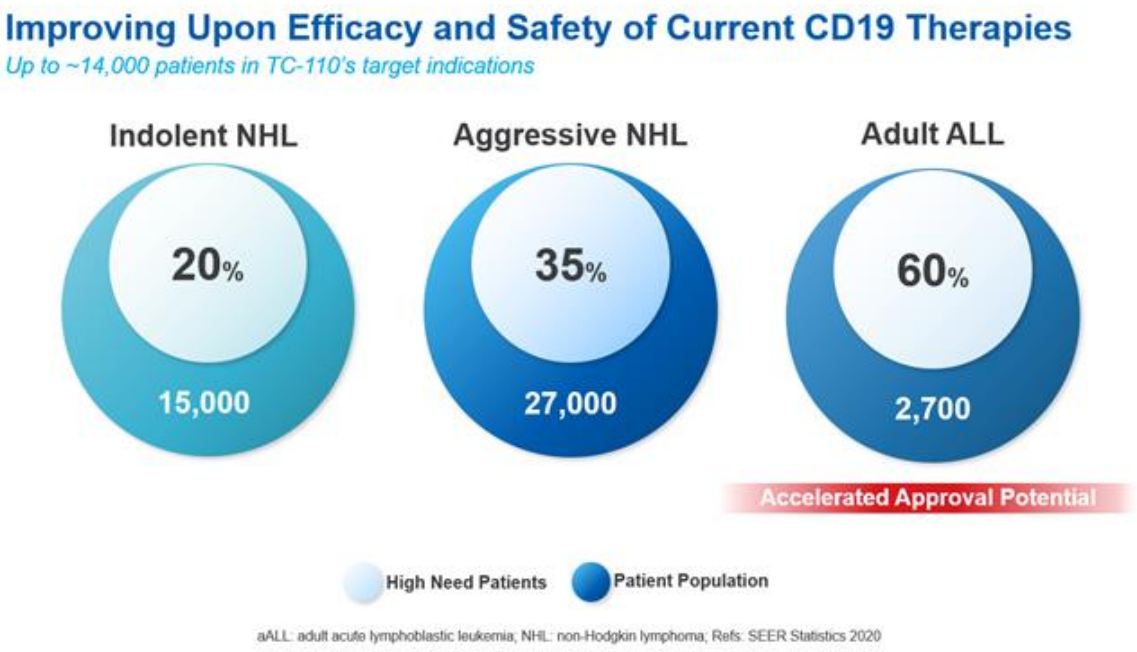
Design of gavo-cel

The construct used to generate gavo-cel is comprised of a humanized single-domain antibody that specifically binds to mesothelin on the cell surface. This binding domain is tethered to the human CD3ε subunit via a flexible linker to form the mesothelin-targeting TRuC construct, as shown below. We use a lentiviral vector to transfer the genetic information for the TRuC construct into a patient's own T cells. Once in the T cell, the TRuC protein is expressed and integrated into the endogenous TCR followed by transport of the reprogrammed TCR to the cell surface. There, it redirects the TRuC-T cells to recognize mesothelin-positive tumor cells and activate them to eliminate mesothelin-positive tumors. We believe that gavo-cel's unique way of engaging and powering T cells as well as its humanized binding domain could lead to improved clinical outcomes for patients. The following figure illustrates the design of gavo-cel.



TC-110: Our Lead Mono TRuC-T Cells Targeting CD19-Positive B-Cell Hematological Malignancies

We are also developing TC-110, a TRuC-T cell targeting CD19-positive B-cell hematological malignancies. The clinical development plan for TC-110 will initially focus on treating patients with adult ALL, DLBCL, FL, and other NHL subtypes. In our preclinical studies, we have observed better anti-tumor activity and persistence of TRuC-T cells compared to CAR-T cells we engineered to target CD19 while also exhibiting lower levels of cytokine release. Based on these preclinical studies, we believe we can improve on the efficacy and safety of current CD19 therapies. We continue to treat patients with TC-110 in the dose escalation portion of the study and anticipate an interim update from the Phase 1 portion of this clinical trial in 2021. We expect to seek FDA Fast Track designation.



Adult ALL Background

ALL is a cancer that results from the malignant proliferation of lymphoid progenitor cells in the bone marrow. It is characterized by an excess of malignant lymphoblasts, which in the vast majority of cases arise from progenitors of the B-cell lineage. In 2020, there were an estimated 6,100 cases of ALL and over 1,500 related deaths in the United States. Adults comprise approximately 45% of all ALL cases but make up more than 85% of ALL-related deaths.

While 80% to 90% of patients with pediatric ALL can be cured with standard therapy and the remaining 10-20% can be effectively treated with allogeneic stem cell transplantation or anti-CD19 CAR-T cell therapy, like Kymriah, the prognosis of adults with ALL is much worse, with a five-year overall survival of 30% to 40%. Furthermore, while Kymriah has been approved for pediatric patients with ALL, no CAR-T cell therapy has been approved in adults with ALL. Thus, the development of T cell therapies in adult patients with ALL will only be possible with platforms that are associated with significantly lower rates of severe CRS and neurotoxicity.

DLBCL Background

Non-Hodgkin lymphomas (NHL) comprise a heterogeneous group of malignancies. DLBCL is the most common subtype of NHL, constituting up to 40% of cases globally. In 2020 there were an estimated 77,000 new cases of NHL and 20,000 related deaths in the United States. Approximately two-thirds of patients with DLBCL are cured of their disease with frontline chemoimmunotherapy (R-CHOP). However, refractory patients have a median overall survival of only 6.3 months.

CD19-directed CAR-T cell therapy has shown activity in heavily pre-treated patients with CD19-positive DLBCL and three CAR-T cell therapies, Kymriah, Yescarta and Breyanzi, have been approved for that indication. However, the response rate six months post-infusion ranges from 37% to 62% and these therapies are associated with high rates of severe CRS (4% to 23%) and neurotoxicity (12% to 28%). Our preclinical data show better anti-tumor activity and lower cytokine release with TC-110 compared to CD28-based or 4-1BB-based CAR-T cells we engineered against CD19-expressing tumors.

Follicular Lymphoma Background

Follicular Lymphoma (FL) is the most common indolent NHL in the Western hemisphere accounting for 20% of patients with newly diagnosed NHL. Approximately 15,000 patients were diagnosed in the United States with FL in 2020. The clinical course of patients with FL is generally indolent, with many patients remaining asymptomatic for months or even years after diagnosis. However, 20% of patients with FL relapse within two years of R-CHOP therapy and have a median five-year survival rate of only 50% compared to 90% for the remaining 80% of patients with a longer response duration.

In 2021, Yescarta was the first approved treatment for adult patients with indolent follicular lymphoma. However, 8% of patients experienced Grade 3 or higher CRS and 21% of patients experienced neurologic events.

Background on Other NHL Subtypes

In addition to DLBCL and FL, we also plan to study TC-110 in patients with other, less common NHL subtypes, including mantle cell lymphoma (MCL) and primary mediastinal B-cell lymphoma (PMBCL). Patients with relapsed/refractory disease in these other NHL subtypes also have a substantial unmet medical need. MCL is an aggressive form of NHL with a median survival of approximately 5 years. PMBCL tends to respond well to initial therapy, but relapsed/refractory patients have a poor prognosis with a reported 25% 2-year survival.

We plan to apply for FDA Fast Track designation, FDA Breakthrough Therapy designation, RMAT and Orphan Drug designations for TC-110, where applicable.

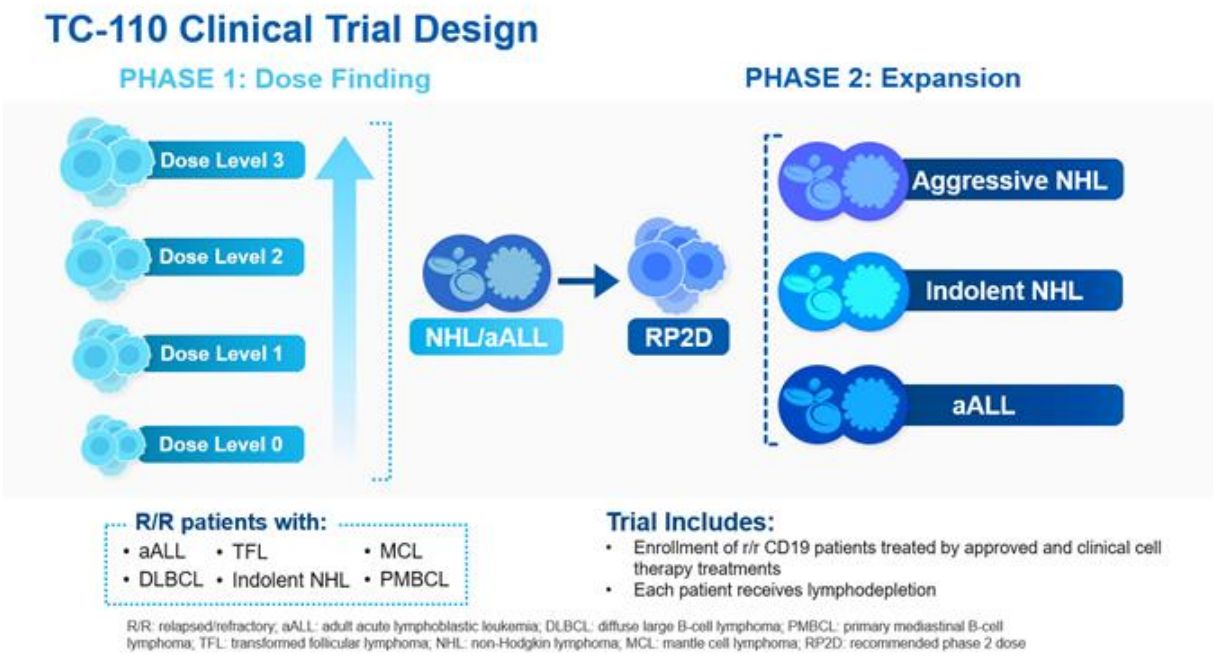
TC-110 Phase 1/2 Trial in CD19-Positive B-Cell Hematological Malignancies

We have initiated a Phase 1/2 clinical trial of TC-110 in patients with CD19-positive B-cell hematological malignancies including adult ALL, DLBCL, FL, and other NHL subtypes. Given the high unmet need and limited treatment options, we plan to apply for FDA Fast Track designation, FDA Breakthrough Therapy designation, RMAT and Orphan Drug designations for TC-110, where applicable.

Our Phase 1/2 clinical trial consists of two parts:

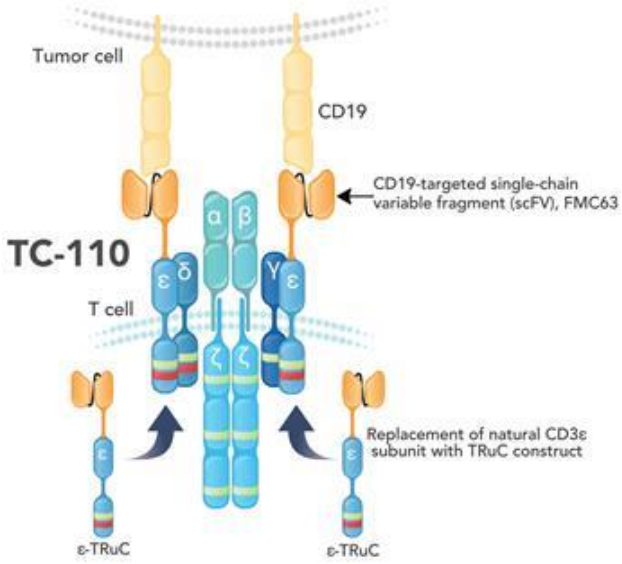
- In the Phase 1 portion of the clinical trial, patients will receive increasing doses of TC-110 T cells following lymphodepleting chemotherapy to determine the recommended Phase 2 dose (RP2D).

- The objective of the Phase 2 portion of the clinical trial, in addition to further characterizing the safety profile of TC-110, is to evaluate the efficacy of TC-110 in CD19-expressing hematological malignancies as assessed by ORR. Secondary endpoints will include time to response, duration of response, progression free survival and overall survival. Approximately 60 patients will receive TC-110 at the RP2D schedule and will be stratified according to their cancer diagnosis in three groups: aggressive NHL, indolent NHL and aALL. Approximately 20 patients per indication will be infused with TC-110 T cells.



Design of TC-110

The construct used to generate TC-110 is comprised of the single chain variable fragment, FMC63, that specifically binds to CD19 on the cell surface that is fused with a flexible linker to the human CD3ε subunit. We use a lentiviral vector to introduce the genetic information of TC-110 into a patient's own T cells. In the cell, the fusion construct is integrated into the natural TCR and transported to the cell surface. The reprogramming of the TCR specificity enables TC-110 to attack and destroy hematological malignancies that are CD19-positive. The following figure illustrates the design of TC-110:



Summary of our Preclinical Data on TC-110

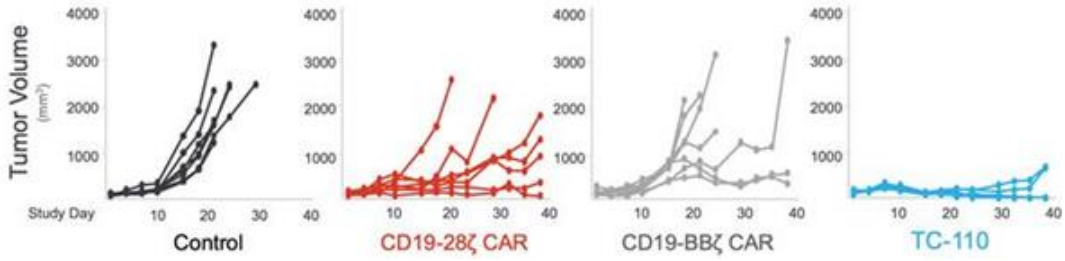
TC-110 showed robust activity in preclinical models where we compared the T cell signaling, cytokine production and anti-tumor activity of TC-110 with CD19-targeting CAR-T cells, which we engineered with the same CD19 binder as TC-110. These CAR-T cells had a similar design as currently used in approved CD19 CAR-T cell therapies but are not identical. Our preclinical data support

our hypothesis that TC-110 could result in potent anti-tumor activity with lower cytokine levels than existing T cell therapies. In our preclinical studies of TC-110, we observed the following results:

- Rapid regression and clearance of tumors in a CD19-positive leukemia model;
- Elimination of tumors in a subcutaneous CD19 lymphoma model; and
- Lower cytokine release compared to CD19-targeting CAR-T cells that we engineered.

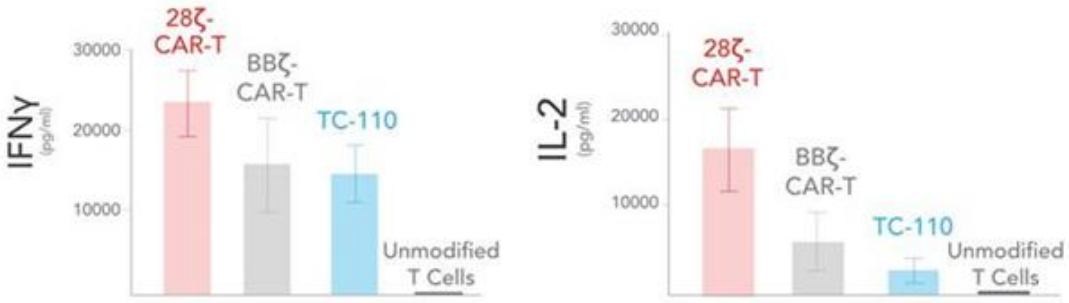
TC-110 cleared subcutaneous lymphoma in a mouse model more efficiently than CAR-T cells

We compared the anti-tumor activity of TC-110 with that of two CD19 CAR-T cells that we engineered to replicate approved CAR-T cell therapies in a subcutaneous lymphoma xenograft model (Raji cell line). Six days after lymphoma cell injection under the skin, mice were treated with similar numbers of either unmodified T cells, TC-110, CD19 CAR-T cells we engineered with a 4-1BB costimulatory domain or CD19 CAR-T cells we engineered with a CD28 costimulatory domain, in each case bearing an identical CD19-binding domain (FMC63). As shown below, treatment with TC-110 resulted in tumor clearance in the majority of mice at the end of the study. In contrast, the CD19 CAR-T cells we engineered were not capable of eradicating the lymphoma cells and despite an initial response, a significant number of animals relapsed. We believe these data support that TC-110 may have a higher and more sustained activity in treating lymphoma than the two CAR-T cell variants. The following figure shows a comparison of the tumor control of TC-110 and the two CAR-T cell variants in the Raji NSG model.



TC-110 releases less cytokines than CAR-T cells

We investigated the effect of TC-110 on cytokine release compared to CAR-T cells we engineered in a cell culture model. CRS is a major safety concern for CAR-T cell therapies. In the model, cytokine levels produced by TC-110 were significantly lower than those released by the CAR-T cells we engineered. These results, as illustrated below, are consistent with the lower levels of cytokine release observed in solid tumor models treated with gavo-cel or the engineered CAR-T cells.



Broadening our Core TRuC-T Cell Platform with a Series of Next-Generation Enhancements

We have developed a novel, transformative platform to address the limitations of existing T cell therapies. Our TRuC-T cell platform is designed to deliver the first HLA-independent TCR-T cell therapies to a broader population of patients with solid tumors and hematological malignancies. Our approach is to fuse a cancer antigen recognition domain directly to a subunit of the TCR, which becomes fully integrated into the natural complex. This has the effect of activating the entire TCR to produce a more powerful, yet controlled T cell response to cancer.

We are focused on continued innovation to broaden our platform through internal research and collaboration with leading academic laboratories and industry partners in the field of T-cell immunology, cell therapy, gene editing, and process development. These innovations fall into three broad categories:

Enhancements

We are developing enhancements that further combat the immunosuppressive solid tumor microenvironment, including mechanisms designed to block a key cancer defense known as the PD-1/PD-L1 pathway. Our lead enhancement is TC-510, our mesothelin targeting TRuC-T cell co-expressing a PD-1:CD28 switch receptor. This switch receptor acts as a cell-intrinsic mechanism to overcome PD-L1/PD-L2 mediated immunosuppression. In our preclinical studies, upon repeated antigen stimulation, co-expression of the switch receptor in mesothelin-targeting T cells enhanced TCR signaling, prevented PD-L1-mediated functional T-cell inhibition, significantly increased proliferation and augmented the production of growth and effector cytokines. We anticipate an IND filing for the TC-510 program targeting mesothelin in 2021.

Our next most advanced enhancement is our IL-15 program followed by our dual TRuC-T cells, TRuCs that target two antigens, to combat heterogeneity in solid tumors and antigen escape in hematological malignancies, a leading mechanism of cancer relapse in patients receiving CAR-T cell therapy.

Allogeneic TRuC-T Cells

We are evaluating proprietary designs for off-the-shelf TRuC-T cells, aiming to give patients faster access to and reduce the costs of TRuC-T cell therapies. In our preclinical studies, we have demonstrated that utilizing our TRuC platform and employing CRISPR endonucleases yielded fully functional TRuC-T cells that lack alloreactivity and upregulated activation markers, secreted cytokines and killed tumors cells in an antigen-specific manner. We anticipate selecting a development candidate for our allogeneic program in 2021 and plan to report preclinical data on our mesothelin-targeted allogeneic TRuC in the first half of 2021.

Novel Targets

Due to the TRuC platform's potential versatility, we believe that we have the capability to target many different cancer antigens and we are focused on the discovery and validation of novel targets to broaden the reach of TRuC-T cells in solid tumors and hematologic cancers. We plan to report preclinical data on our TRuC-T cell targeting CD70 in the first half of 2021.

Manufacture and Delivery of TRuC-T Cells to Patients

TRuC-T Cell Production and Delivery

The process of manufacturing cell and gene therapies, such as TRuC-T cells, is highly complex. As shown in the figure below, the generation of our TRuC-T cells starts with the collection of white blood cells from patients, known as leukapheresis, at the treatment center. The blood cells are shipped to a central manufacturing facility where they are further processed. Following the enrichment of the sample T cells, they are activated, which causes them to divide. In the next step, a viral vector is used to shuttle the genetic information encoding the TRuC construct into the T cells. During the assembly process of the TCR, the TRuC construct is integrated into the natural TCR complex and transported to the cell surface. The now reprogrammed TRuC-T cells are further stimulated to replicate and produce enough quantities to administer a therapeutic dose to the patient from whom the cells were originally collected.

We use a next-generation cell processing platform that performs cell sample loading, cell washing, density-based cell separation, magnetic separation, cell culture and final product formulation. This is a semi-automated and functionally closed system that we believe will enable us to scale our TRuC-T cell manufacturing and overcome the constraints associated with current processes.

TRuC-T Cell Manufacturing Strategy

We are devoting extensive resources to process development and manufacturing to optimize the reliability of our product candidates and reduce manufacturing costs and vein-to-vein time. This investment will ensure that our manufacturing and delivery process will have utility across all the product candidates in our pipeline.

The generation of a genetically-modified autologous T cell therapy such as TRuC-T cells involves several integrated and complex steps, including the collection of T cells through apheresis, cryopreservation, manufacture of the transfer vector under cGMP conditions, *ex vivo* selection, activation, transduction, and expansion of the TRuC-T cells, ultimately leading to infusion of TRuC-T cells into patients. The technical, logistical, and regulatory challenges associated with the virus and cell manufacturing processes are significant. We plan to simplify the manufacturing process through the implementation of automated technologies and the development of scalable processes aimed at reducing the cost of goods.

We have already taken two critical steps geared towards simplifying our manufacturing process. First, our TRuC-T cells are manufactured via a semi-automated and functionally closed system (CliniMACS Prodigy), which provides a common platform that will be employed in the development of all of the product candidates in our pipeline. This manufacturing process is economical, reliable, and scalable, and can support rapid development of the product candidates throughout the clinical life cycle and regulatory approvals. This system has a small footprint, which enables us to manufacture multiple products in parallel units within the same

minimally controlled space, thereby reducing operating costs. Second, both the input leukapheresis material that enters the manufacturing process as well as the final TRuC-T cells are cryopreserved products, which simplifies the logistics for delivery to the patient and reduces the risk of product delivery failure. The entire vein-to-vein manufacturing process has safe-guards in place designed to ensure product identity and integrity throughout the production life-cycle.

We have entered into manufacturing agreements for the supply of GMP-S plasmids for generation of the viral vectors, which are manufactured by third parties. The viral vectors are manufactured through established agreements with various CDMOs. We outsource our T cell manufacturing process and we may enter into additional agreements to increase capacity for future clinical trials and commercialization if licensed. Because our starting materials are frozen, we expect to be able to base future agreements on rolling forecasts of regularly scheduled manufacturing runs, which we expect will minimize any cost overruns due to loss of reservation fees. Depending on the results of our clinical trials, we may choose to develop our own manufacturing capabilities.

As part of our manufacturing strategy, we plan to expand our capacity as we continue our existing clinical trials and begin additional clinical trials and are planning for potential further expansion in anticipation of an approval for any of our TRuC-T cell product candidates.

Under our existing agreements with CDMOs, we estimate that we have potential access to capacity to produce up to approximately 100 annual treatments per year, which we believe will be sufficient to conduct our initial planned clinical trials. We are in the process of adding manufacturing capacity to support larger clinical trials for our product candidates.

In December 2018, we contracted with Cell Therapy Catapult Limited, United Kingdom to occupy a suite with our own personnel and equipment in their GMP manufacturing center in Stevenage, United Kingdom. Our UK manufacturing suite is now operational, and we expect our manufacturing suite to be MHRA certified in the middle of 2021. We estimate the UK facility operating at full capacity expands our manufacturing capacity to a total of up to 300 treatments per year and facilitates conducting clinical trials in the United States and Europe. Additionally, we intend to apply our learnings from Catapult towards our own future commercial manufacturing.

In November 2020, we contracted with ElevateBio, LLC, to leverage the extensive technical capabilities at ElevateBio BaseCamp, a world-class cell and gene therapy manufacturing facility based in Waltham, MA. Elevate BaseCamp was established as a center of innovation dedicated to cell and gene therapy research and development, process development and cGMP manufacturing operations, using state-of-the-art facilities designed to rapidly develop single and multi-product cell and gene therapies, regenerative medicine and immunotherapies. The BaseCamp partnership enables TCR^2 Therapeutics to utilize our own equipment in close proximity to our U.S. headquarters in Cambridge, MA and establish additional manufacturing capacity and technical capabilities in the U.S. and will support the Phase 2 expansion portion of the gavo-cel Phase 1/2 clinical trial once a recommended Phase 2 dose is defined. Additionally, we intend to apply our learnings from ElevateBio towards our own future commercial manufacturing.

If our clinical trials are successful, we plan to acquire and develop our own manufacturing infrastructure to generate the additional capacity needed to support expanded clinical trials and commercial scale production. We believe our manufacturing platform can be scaled with minimal infrastructure while meeting GMP requirements, which will facilitate the design and building of a standard centralized manufacturing facility. Further into the future, however, we expect this system to be amenable to manufacturing in a controlled non-classified environment closer to or at the point of care, such as at a regional hub or hospital, resulting in a decentralized manufacturing model. We anticipate that this decentralized model would require minimal infrastructure, be led by operators that would require minimal technical training, shorten vein-to-vein time, and decrease costs.

Intellectual Property

Intellectual property is a fundamental component of our business and of vital importance in our field. We actively seek to protect the intellectual property and proprietary technology that we believe is important to our business, including seeking, maintaining, enforcing and defending patent rights for our product candidates and processes, whether developed internally or licensed from third parties. We may additionally rely on regulatory protection afforded through orphan drug designations, data exclusivity, market exclusivity, and patent term extensions where available.

The TRuC-T cell platform was initially conceived and developed by our scientific founder, Dr. Patrick Baeuerle. The priority patent application disclosing the TRuC-T cell platform was filed in May 2015. Our further work encompassing a broad range of TRuC concepts has been described in subsequent patent applications.

Additional patent applications filed by us since 2015 include at least the following additional technological innovations and product-related claims:

- TRuC-T cells targeting an array of tumor antigens;
- TRuC-T cells targeting multiple types of antigens on the same tumor;
- engineered TRuC-T cells with enhanced activity and/or modulated activity;
- second generation off-the-shelf TRuC-T cells;

- methods of generating TRuCs with enhanced efficacy; and
- methods of using TRuC-T cells to treat human diseases, including solid tumors.

Our strategy is to pursue a variety of broad claims in the United States and foreign jurisdictions to provide multiple layers of patent protection, including:

- pursuing broad claims in the United States for the TRuC concept
- pursuing claims to specific compositions of matter in connection with particular TRuC constructs (including specific protein and nucleic acid sequences)
- methods of generating TRuCs; and
- methods of using the TRuC-T cell platform as monotherapy or in combination with other anti-cancer or immune system enhancing therapeutics.

Many of the patent applications that we own or in-license, including our trademark filings, are still in the early stages of prosecution and no claims have been issued yet, with the exception of five issued U.S. patents and eight issued foreign patents. Examination of many of the patent applications that we own has not yet commenced, because they are either provisional applications or Patent Cooperation Treaty (PCT) applications that are not examined. We will need to decide whether and where to pursue protection for the inventions disclosed in these provisional and PCT applications before applicable statutory deadlines, our applications will only be examined in jurisdictions where we elect to pursue protection, and we will only have the opportunity to attempt to obtain patents in such jurisdictions where we elect to pursue protection. We are seeking protection across a range of commercially important territories, including (but not limited to) countries in North America, Europe, and Asia. As of March 1, 2021, our patent portfolio includes five issued U.S. patent, at least 28 pending U.S. provisional or nonprovisional patent applications, at least six pending Patent Cooperation Treaty (PCT) international applications, eight issued foreign patents, and at least 101 pending foreign patent applications, which patent applications we own or in-license. The claims of these patent applications are directed toward various aspects of our product candidates and research programs including compositions of matter, methods of use, and processes. These owned and in-licensed patents and patent applications, if issued, are expected to expire on various dates from 2036 through 2042, in each case without taking into account any possible patent term adjustments or extensions.

Within our patent portfolio, as of March 1, 2021, we owned two issued U.S. patents, at least 14 pending U.S. provisional or U.S. nonprovisional patent applications, at least four pending PCT international applications, six issued foreign patents, and at least 60 pending foreign patent applications, and had a nonexclusive license from Harpoon Therapeutics, Inc. (Harpoon) to one U.S. patent, at least one pending U.S. nonprovisional patent application, and had an non-exclusive license to at least ten pending foreign patent applications that include claims directed to gavo-cel, such as compositions of matter, manufacturing methods, manufacturing precursors or uses thereof. These owned and in-licensed patents and patent applications, if issued, are expected to expire on various dates from 2036 through 2041, in each case without taking into account any possible patent term adjustment or extensions.

Within our patent portfolio, as of March 1, 2021, we owned at least two issued U.S. patents, at least nine pending U.S. provisional or U.S. nonprovisional patent application, at least three pending PCT international applications, three issued foreign patents, and at least 34 pending foreign patent applications that include claims directed to TC-110, such as compositions of matter, manufacturing precursors or uses thereof. These owned and in-licensed patents and patent applications, if issued, are expected to expire on various dates from 2036 through 2041, in each case without taking into account any possible patent term adjustment or extensions.
Our trademark portfolio currently contains issued trademarks for TCR2, TRuC, and our logo in the United States.

Collaborations and Licenses

Harpoon License

In June 2017, we entered into a license with Harpoon (the Harpoon License) that grants us a perpetual, irrevocable, world-wide, non-exclusive, royalty free, sublicensable license to research, develop, make, use, sell, commercialize or otherwise exploit products based on Harpoon's MSLN polypeptide binding proteins (the MSLN Binder). We have incorporated the MSLN Binder into gavo-cel.

As consideration for the Harpoon License, we granted Harpoon a perpetual, irrevocable, world-wide, non-exclusive, royalty free, sublicensable license to research, develop, make, use, sell, commercialize or otherwise exploit products based on certain binding proteins which we had developed (the Out-Licensed Binder). We do not incorporate the Out-Licensed Binder into any of our product candidates.

Under the Harpoon License, we retain ownership of the Out-Licensed Binder and own any of our improvements to the MSLN Binder and any of our product candidates incorporating the MSLN Binder. Similarly, Harpoon retains ownership of the MSLN Binder and owns any of its improvements to the Out-Licensed Binder and any of its products incorporating the Out-Licensed Binder. Each party is responsible for the prosecution and maintenance of the patent rights owned by such party.

The Harpoon License is effective through the expiration of all patents underlying the MSLN Binder and Out-Licensed Binder and it may be terminated by either party upon a material breach that remains uncured for 60 days after receiving notice thereof, or in the event of the other party's bankruptcy.

Cell Therapy Catapult Limited Collaboration Agreement

On December 18, 2018, we entered into a Collaboration Agreement with Cell Therapy Catapult Limited (Catapult) to establish our GMP manufacturing and supply chain at their GMP manufacturing center in Stevenage, United Kingdom. The agreement also provides us with an option to expand our collaboration area with a second GMP cleanroom suite in Catapult's second phase of development. The agreement is for a term of three years with earlier termination available to us on provision of twelve months' notice. Termination is also possible in the event of material breach of the Agreement that remains uncured for 90 days and insolvency of a party.

The Catapult manufacturing center is a GMP facility. The agreement will enable us to have our own dedicated manufacturing space in the Catapult manufacturing center. Catapult's contribution to collaboration is their GMP support, expertise, and inbound and outbound logistics and supply chain, being developed at the center. We will use our own manufacturing process and we will be responsible for the operation of the manufacturing process in the suite.

ElevateBio

In November 2020, we announced a partnership with ElevateBio, LLC, or ElevateBio, a Cambridge, MA-based creator and operator of a portfolio of innovative cell and gene therapy companies. The agreement with ElevateBio provides us access to ElevateBio BaseCamp, its centralized 140,000 square foot, world-class cell and gene therapy manufacturing facility based in Waltham, MA. The BaseCamp partnership enables us to establish additional manufacturing capacity and technical capabilities in the United States manufacturing facility, and will support the Phase 2 expansion portion of the gavo-cel Phase 1/2 clinical trial once a recommended Phase 2 dose is defined.

Competition

We believe our novel TRuC-T cell platform, its design flexibility, superior performance over CAR-T cell and TCR-T cell therapies, emerging enhancements, and our knowledge of cellular immunotherapy should enable us to successfully develop novel and highly effective treatments for cancer. However, we may face intense and increasing competition from larger biotechnology and pharmaceutical companies with greater financial resources, who are also developing immuno-oncology therapies (including cellular therapies) and more traditional treatments for cancer. In addition, academic institutions, governmental agencies, public and private research institutions, and early stage or smaller companies could also prove competitive.

The market opportunity in oncology has led to a number of collaborations GlaxoSmithKline plc (GlaxoSmithKline)/Adaptimmune Therapeutics PLC (Adaptimmune), Janssen Biotech, Inc. (Janssen)/ Nanjing Legend Pharmaceutical & Chemical Co., Ltd (Legend), bluebird bio, Inc. (bluebird)/ Regeneron Pharmaceuticals Inc. (Regeneron) and bluebird/Gritstone Oncology, Inc.) and major acquisitions (Gilead Sciences, Inc. (Gilead)/Kite Pharma Inc. (Kite), Bristol Myers Squibb Co (BMS)/Celgene Corporation (Celgene)/Juno Therapeutics, Inc. (Juno)) among companies focused on cellular cancer therapies. If this trend continues, which we expect, we could see further consolidation of technical expertise and human capital. This potentially provides a partnership opportunity for us but could also make it more challenging for us to acquire complementary technology or products and recruit and retain qualified scientific and management personnel. In addition, this competition could impact our ability to recruit clinical trial sites and patients in a timely manner for our clinical trials. Larger companies with greater financial flexibility and global reach may be able to obtain regulatory approvals and gain widespread market acceptance before us, which could impact our commercial launch and could make our products obsolete or non-competitive.

We are developing one of our lead product candidates, gavo-cel, in combination with an immune checkpoint inhibitor for the treatment of NSCLC. Others are evaluating these immune checkpoint inhibitor approaches in combination with CAR-T cells and TCR-T cells to enhance efficacy in the treatment of solid tumors and hematological malignancies. We therefore could experience significant direct competition from this type of combination immunotherapy. We may also face substantial competition in the future from other immunotherapies, if their use alone or in combination demonstrates a significant improvement in efficacy. Development of more effective small molecules, antibody-based approaches, cancer vaccines, oncolytic viruses and other products could lead to them preferentially being used as first- or second-line treatments, which would reduce the opportunity for our product candidates.

Despite the unique approach that we have developed to address the limitations of CAR-T cells and TCR-T cells, we expect to face increasing competition as new more effective treatments for cancer enter the market and further advancements in technologies are made. We expect market adoption of any treatments that we develop and commercialize to be dependent on, among other things, efficacy, safety, delivery, price and the availability of reimbursement from government and other third-party payors.

We expect the commercial opportunity for our products that we take to regulatory licensing to be reduced or eliminated if competitors develop and commercialize products that are more effective, safer (have fewer or less severe side effects), are more convenient or

are less expensive or better reimbursed than any products that we may commercialize. We compete with larger, better-funded companies, who may obtain regulatory approval for their products more rapidly than we may obtain licensing for ours. This could result in our competitors establishing a strong market position for either the product or a specific indication before we are able to enter the market.

Competition for Our Product Candidates Targeting Mesothelin-Expressing Solid Tumors

The overexpression of mesothelin by numerous solid tumors, combined with its low expression on mesothelial cells lining the pleura, peritoneum, and pericardium, has led to a number of different mesothelin-targeting agents being tested in Phase 1/2 trials. These approaches include novel antibody therapeutics, such as unconjugated monoclonal antibodies, antibody-drug conjugates, bispecific antibodies as well as vaccines. Antibody-based approaches are being pursued by F. Hoffmann-La Roche Ltd, Bayer AG, Bristol-Myers Squibb Company, Selecta Biosciences, Inc., Novimmune SA, Harpoon Therapeutics, Inc., Amgen Inc., and Morphotek, Inc., among others. Antibody-based agents in development have been limited to date by immunogenicity, poor tumor penetration and dose-limiting toxicities associated with the therapy. Tmunity Therapeutics, Inc., Atara Biotherapeutics, Inc., Memorial Sloan Kettering Cancer Center, the National Institutes of Health Clinical Center, Maxcyte, Inc., Legend Biotech Corp, Gracell Biotechnology Inc., CARISMA Therapeutics Inc., Refuge Biotechnologies, Inc., Adaptimmune Therapeutics PLC, Kiromic Biopharma, Inc. and several Chinese academic institutions are developing anti-mesothelin cell therapies.

Competition for Our Product Candidates Targeting CD19-Positive Hematological Malignancies

Recent regulatory approvals of Gilead's, Novartis' and Bristol-Meyers Squibb's CAR-T cell therapies have led a number of companies to increase their research and development efforts in the cell therapeutics field, including Janssen through its collaboration with Legend, as well as the entry into the field by many other companies. In addition to these CAR-T cell therapies, many companies are developing enhanced cell therapies, which may compete with TC-110. These include Cellectis S.A./Allogene Therapeutics, Inc., Mustang Bio, Inc., Autolus Therapeutics plc, Crispr Therapeutics AG, Precision BioSciences, Inc., Sana Biotechnology, Inc., Eureka Therapeutics, Inc., Triumvira Immunologics, Inc., Poseida Therapeutics, Inc., Takeda Pharmaceutical Co Ltd, Fate Therapeutics Inc., and Miltenyi Biotec GmbH, among others. Companies such as F. Hoffmann-La Roche Ltd, Genmab A/S, Amgen Inc., Xencor Inc., Regeneron, ADC Therapeutics SA, MorphoSys AG, IGM Biosciences, Inc., Forty Seven, Inc., and others are pursuing antibody based approaches. We therefore expect competition within the cell therapy field to intensify and for antibody-based approaches to more directly compete with cell therapies in the future.

Government Regulation and Product Licensure

Government authorities in the United States, at the federal, state, and local level, and in other countries and jurisdictions, including the EU, extensively regulate, among other things, the research, development, testing, manufacture, pricing, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of biopharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Licensure and Regulation of Biologics in the United States

In the United States, biological products such as our lead product candidates, are licensed for marketing by the FDA under the Public Health Service Act (PHSA), and regulated by the FDA under the Federal Food, Drug, and Cosmetic Act (FDCA), as well as by other federal, state and local statute and regulations. Both the FDCA and the PHSA and their corresponding regulations govern, among other things, the testing, manufacturing, safety, potency, labeling, packaging, storage, record keeping, distribution, reporting, advertising, and other promotional practices involving biological products. The FDA must license a biological product before it may be marketed within the United States. Within the FDA, the Center for Biologics Evaluation and Research (CBER) regulates cell therapy products.

The failure of an applicant to comply with the applicable regulatory requirements at any time during the product development process, including non-clinical testing, clinical testing, the approval process or post-approval process, may result in delays to the conduct of a study, regulatory review and approval, and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the FDA's refusal to allow an applicant to proceed with clinical trials, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, and civil or criminal investigations and penalties brought by the FDA or Department of Justice (DOJ), or other government entities, including state agencies.

An applicant seeking licensing to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps before the product candidate will be licensed by the FDA.

- preclinical testing including laboratory tests, animal studies, and formulation studies, which must be performed in accordance with the FDA's good laboratory practice (GLP) regulations and standards;
- submission to the FDA of an Investigational New Drug application (IND) for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an institutional review board (IRB) representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency, and purity of the product candidate for each proposed indication, in accordance with current good clinical practices (GCP);
- preparation and submission to the FDA of a BLA for a biological product 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 for one or more proposed indication(s) and the payment of user fees (unless exempt);
- FDA acceptance and substantive review of the BLA;
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities, including those of third parties, at which the product candidate or components thereof are manufactured to assess compliance with cGMP requirements and to assure that the facilities, methods, and controls are adequate to preserve the product's identity, strength, quality, and purity;
- satisfactory completion of any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCP and the integrity of clinical data in support of the BLA;
- securing FDA licensure of the BLA to allow marketing of the new biological product; and
- compliance with any post-licensing requirements, including the potential requirement to implement a REMS and the potential requirement to conduct and any post-licensing studies required by the FDA.

Preclinical Studies and Investigational New Drug Application

Before an applicant begins testing a product candidate with potential therapeutic value in humans, the product candidate enters preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, formulation, and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA a part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved BLA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, must be submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval or licensing. In particular, such studies must be conducted in accordance

with GCP, including review and approval by an independent ethics committee (IEC) and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies and the FDA must be able to validate the data through an onsite inspection, if deemed necessary by the FDA. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee (DSMB). This group provides authorization as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website.

Additional Regulation for Gene Therapy Clinical Trials

In addition to the regulations discussed above, there are a number of additional standards that apply to clinical trials involving the use of gene therapy. The FDA has issued various guidance documents regarding gene therapies, which outline additional factors that the FDA will consider at each of the above stages of development, which relate to, among other things: the proper preclinical assessment of gene therapies; the CMC information that should be included in an IND; the proper design of tests to measure product potency in support of an IND or BLA; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. Further, the FDA usually recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by ten years of annual queries, either in person or by questionnaire, although the FDA recently proposed updating its guidance on long-term follow-up after administration of human gene therapy products.

The NIH and the FDA have a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene therapy trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events on these trials.

Human Clinical Trials in Support of a BLA

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of a qualified investigator in accordance with GCP requirements which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written clinical trial protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may also be required after licensing.

- Phase 1 clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics in healthy humans or in patients. During Phase 1 clinical trials, information about the investigational biological product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.
- Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the potency or efficacy of the product candidate for specific targeted indications, and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. Phase 2 clinical trials are well controlled, closely monitored and conducted in a limited patient population.

- Phase 3 clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially potent or effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical potency or efficacy, and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to license, and, if licensed, how to appropriately label a biologic. Such Phase 3 studies are referred to as “pivotal.”

In some cases, the FDA may approve a BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate’s safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group and to further document a clinical benefit in the case of biologics licensed 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 must be submitted at least annually to the FDA. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the case 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, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB’s requirements or if the product has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Clinical trials sometimes require submission of an application for an Investigational Device Exemption, or IDE, to the FDA. The IDE application, when requested, must be supported by appropriate data, such as animal and laboratory testing results, showing that it is safe to test the device in humans and that the investigational protocol is scientifically sound. The IDE application must be approved in advance by the FDA, unless the product is deemed a non-significant risk device and eligible for more abbreviated IDE requirements. Clinical trials for a significant risk device may begin once the IDE application is approved by the FDA as well as the appropriate institutional review boards, or IRBs, at the clinical trial sites, and the informed consent of the patients participating in the clinical trial is obtained.

Review and Approval of a BLA

In order to obtain approval to market a biological product in the United States, a marketing application must be submitted to the FDA that provides sufficient data establishing the safety, purity and potency of the proposed biological product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product’s chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of 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, purity and potency of the biological product to the satisfaction of the FDA.

The BLA is a vehicle through which applicants formally propose that the FDA license a new product for marketing and sale in the United States for one or more indications. Every new biological product candidate must be the subject of an approved BLA before it may be commercialized in the United States. Under federal law, the submission of most BLAs is subject to a significant application user fee. The sponsor of an approved BLA is also subject to an annual program fee. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of a BLA, the FDA conducts a preliminary review of the application generally within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA’s receipt of the submission whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept the application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of the BLAs. Under that agreement, 90% of original BLA submissions are meant to be reviewed within ten months of the 60-day filing date, and 90% of original BLAs that have been designated for “priority review” are meant to be reviewed within six months of the 60-day filing date. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider

new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with a BLA submission, including component manufacturing, finished product manufacturing and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events and whether the product is a new molecular entity.

The FDA may refer an application for a novel product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides 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.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Medical Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as Fast Track designation, Breakthrough Therapy designation, Priority Review designation and Regenerative Medical Advanced Therapy designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if licensed, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

A product may be designated as a regenerative medicine advanced therapy if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative medicine advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality (IMM) and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. Thus, the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

The accelerated approval pathway is usually contingent on a sponsor’s agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product’s clinical benefit. As a result, a product candidate licensed on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the product. All promotional materials for product candidates licensed under accelerated regulations are subject to prior review by the FDA.

The FDA’s Decision on a BLA

On the basis of the FDA’s evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA’s satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for licensing.

If the FDA licenses a new product, it may limit the licensed indications for use of the product. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for health care professionals, and elements to assure safe use (ETASU). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After licensing, many types of changes to the licensed product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Licensing Regulation

If regulatory licensing for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-licensing regulatory requirements as well as any post-licensing requirements that the FDA may have imposed as part of the licensing process. The sponsor will be required to report, among other things, certain adverse reactions and

manufacturing problems to the FDA, provide updated safety and potency or efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Changes to the manufacturing processes are strictly regulated and often require prior FDA approval before being implemented. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency, and effectiveness of pharmaceutical products.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market, or product recalls;
- fines, warning letters, or holds on post-licensing clinical trials;
- refusal of the FDA to approve pending applications or supplements to licensed applications, or suspension or revocation of product license licenses;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is licensed. After licensing, a drug product generally may not be promoted for uses that are not licensed by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services (HHS), as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (PDMA) and its implementing regulations, as well as the Drug Supply Chain Security Act (DSCSA), which regulate the distribution and tracing of prescription drug samples at the federal level, and set minimum standards for the regulation of distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act, a BLA or supplement thereto for a biological product with a new active ingredient, indication, dosage form, dosing regimen or route of administration must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and

administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

For products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with sponsors and FDA must meet with sponsors by no later than the end-of-Phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after licensing of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

The FDA Reauthorization Act of 2017 established new requirements to govern certain molecularly targeted cancer indications. Any company that submits a BLA three years after the date of enactment of that statute must submit pediatric assessments with the BLA if the biologic is intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary potency to inform pediatric labeling for the product. Deferrals and waivers as described above are also available.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot license another application.

Orphan Drug Designations and Exclusivity

Under the Orphan Drug Act, the FDA may designate a biological product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a product available in the United States for treatment of disease or condition will be recovered from sales of the product. A company must seek orphan drug designation before submitting a BLA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and licensing process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not license another sponsor's marketing application for the same drug for the same condition for seven years, except in certain limited circumstances. Orphan exclusivity does not block the licensing of a different product for the same rare disease or condition, nor does it block the licensing of the same product for different conditions. If a biologic designated as an orphan drug ultimately receives marketing licensing for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar licensing of another product under certain circumstances, including if a subsequent product with the same biologic for the same condition is shown to be clinically superior to the licensed product on the basis of greater potency, purity or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Biosimilars and Exclusivity

The 2010 Patient Protection and Affordable Care Act, which was signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCIA). The BPCIA established a regulatory scheme authorizing the FDA to license biosimilars and interchangeable biosimilars. The FDA has licensed several biosimilar products for use in the United

States. The FDA has issued several guidance documents outlining an approach to review and licensing of biosimilars. Additional guidances are expected to be proposed and finalized by the FDA in the near term.

Under the BPCIA, a manufacturer may submit an application for licensure of a biological product that is "biosimilar to" or "interchangeable with" a previously licensed biological product or "reference product." In order for the FDA to license a biosimilar product, it must find, among other things, that the product is "highly similar" to the reference product notwithstanding minor differences in clinically inactive components and that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to license a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and, for products administered multiple times, that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished potency relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar or interchangeable biological product may not be submitted to the FDA until four years following the date of licensing of the reference product. The FDA may not license a biosimilar or interchangeable biological product until 12 years from the date on which the reference product was licensed. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA licenses a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars licensed as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Patent Term Restoration and Extension

A patent claiming a new biological product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of an IND and the submission date of a marketing application (such as a BLA), plus the time between the submission date of a marketing application and the ultimate licensing date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's licensing date. Only one patent applicable to a licensed product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question and within 60 days after approval of the relevant marketing application. A patent that covers multiple products for which licensing is sought can only be extended in connection with one of the licenses. The USPTO reviews and licenses the application for any patent term extension or restoration in consultation with the FDA.

Healthcare Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of biological products that are granted marketing licensing. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other health care laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state health care laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and wilfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid. Moreover, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act. On December 2, 2020, the Office of Inspector General, or OIG, published further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. This rule (with exceptions) became effective January 19, 2021. Implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be further amended or repealed;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which created additional federal criminal laws that prohibit, among other things, knowingly and wilfully executing, or attempting to execute, a scheme to defraud any health care benefit program or making false statements relating to health care matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute, which prohibits knowingly and wilfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for health care benefits, items or services;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the 2010 Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act (collectively, the ACA), which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services (CMS) within the HHS, information related to payments and other transfers of value made by that entity to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made during the previous year to certain non-physician providers such as physician assistants and nurse practitioners; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to health care items or services that are reimbursed by non-government third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. In addition, certain state and local laws require the registration of pharmaceutical sales representatives. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pharmaceutical Insurance Coverage and Health Care Reform

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products. Thus, even if a product candidate is licensed, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is licensed. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on a licensed list, also known as a formulary, which might not include all of the licensed products for a particular indication.

In order to secure coverage and reimbursement for any product that might be licensed for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing licenses. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is licensed and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be licensed. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any licensed products. 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 a company or its collaborators receive marketing licenses, less favorable coverage policies and reimbursement rates may be implemented in the future.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States. In March 2010, the ACA was enacted, which includes measures that have significantly changed health care financing by both governmental and private insurers. The provisions of the ACA of importance to the pharmaceutical and biotechnology industry are, among others, the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drug agents or biologic agents, which is apportioned among these entities according to their market share in certain government health care programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- requirements under the federal Physician Payments Sunshine Act for drug manufacturers to report information related to payments and other transfers of value made to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made during the previous year to certain non-physician providers such as physician assistants and nurse practitioners;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- establishment of the Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Other legislative changes have been proposed and adopted since the ACA was enacted. For example, the Budget Control Act of 2011, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and will stay in effect through 2030 unless additional Congressional action is taken. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, as well as subsequent legislation, these reductions have been suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. Proposed legislation, if passed, would extend this suspension until the end of the pandemic. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory licensing or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

These healthcare reforms, 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 additional downward pressure on the price for any licensed product and/or the level of reimbursement physicians receive for administering any licensed product. Reductions in reimbursement levels may negatively impact the prices or the frequency with which products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the United States Supreme Court; the former Trump Administration issued various Executive Orders which eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices; and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. The United States Supreme Court is expected to rule on a legal challenge to the constitutionality of the ACA in

early 2021. The implementation of the ACA is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Litigation and legislation related to the ACA are likely to continue, with unpredictable and uncertain results.

Further, 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 programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress has indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care 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 health care programs. These measures could reduce the ultimate demand for our product candidates, once licensed, or put pressure on our product pricing.

The former Trump administration’s budget proposal for fiscal year 2021 included a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the former Trump administration sent “principles” for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. The former Trump administration also previously released a “Blueprint” to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. HHS has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. It is unclear whether the Biden administration will challenge, reverse, revoke or otherwise modify these executive and administrative actions after January 20, 2021.

In 2020, former President Trump announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. In response, the FDA released a final rule 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. 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 will 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. The MFN Model regulations mandate participation by identified Part B providers and would have applied to all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. However, in response to a lawsuit filed by several industry groups, on December 28, the U.S. District Court for the Northern District of California issued a nationwide preliminary injunction enjoining government defendants from implementing the MFN Rule pending completion of notice-and-comment procedures under the Administrative Procedure Act. On January 13, 2021, in a separate lawsuit brought by industry groups in the U.S. District of Maryland, the government defendants entered a joint motion to stay litigation on the condition that the government would not appeal the preliminary injunction granted in the U.S. District Court for the Northern District of California and that performance for any final regulation stemming from the MFN Interim Final Rule shall not commence earlier than 60 days after publication of that regulation in the Federal Register. Further, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada and the MFN Model may materially and adversely affect the price we receive for any of our product candidates. Additionally, on December 2, 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 an order entered by the U.S. District Court for the District of Columbia, the portion of the rule eliminating safe harbor protection for certain rebates related to the sale or purchase of a pharmaceutical product from a manufacturer to a plan sponsor under Medicare Part D has been delayed to January 1, 2023. Implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed.

Review and Approval of Medicinal Products in the EU

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA licensing for a product, an applicant will need to obtain the necessary approvals by the comparable non-U.S. regulatory authorities before it can commence

clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the EU generally follows the same lines as in the United States although the approval of a medicinal product in the United States is no guarantee of approval of the same product in the European Union, either at all or within the same timescale as approval may be granted in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application (MAA), and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on GCP and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the EU. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion in relation to the clinical trial. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC and, where relevant, the implementing national provisions of the individual EU Member States and applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted. The Regulation was published on June 16, 2014 but is not expected to come into effect until late 2020 at the earliest. It is expected that the Clinical Trials Regulation will apply following confirmation of full functionality of the Clinical Trials Information System (CTIS), the centralized EU portal and database for clinical trials foreseen by the regulation, through an independent audit. The regulation becomes applicable six months after the European Commission publishes notice of this confirmation. The Clinical Trials Regulation will be directly applicable in all the EU Member States - meaning that no national implementing legislation will be required - and it will supersede and repeal the current Clinical Trials Directive 2001/20/EC and any national legislation that was put in place to implement the Directive. Conduct of all clinical trials performed in the EU will continue to be governed by the Clinical Trials Directive and national implementing legislation until the new Clinical Trials Regulation becomes applicable. The extent to which on-going clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. Clinical trials applications made before the entry into force of the Clinical Trials Regulation will continue to be governed by the Clinical Trials Directive for up to three years after the Clinical Trials Regulation becomes applicable, as will clinical trials applications made within one year of the Clinical Trials Regulation becoming applicable where the clinical trial sponsor elects for the trial to be governed by the old regime until the end of the three year transition period. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the “EU Portal and Database”; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting Member State, whose assessment report is submitted for review by the sponsor and all other competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (the so-called Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the Member State concerned. However, overall related timelines will be defined by the Clinical Trials Regulation.

PRIME Designation in the EU

EMA now offers a scheme that is intended to reinforce early dialogue with, and regulatory support from, EMA in order to stimulate innovation, optimize development and enable accelerated assessment of PRIority MEdicines (“PRIME”). It is intended to build upon the scientific advice scheme and accelerated assessment procedure offered by EMA. The scheme is voluntary and eligibility criteria must be met for a medicine to qualify for PRIME.

The PRIME scheme is open to medicines under development and for which the applicant intends to apply for an initial marketing authorization application through the centralized procedure. Eligible products must target conditions for which where is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the European Union or, if there is, the new medicine will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods or therapy or improving existing ones. Applicants will typically be at the exploratory clinical trial phase of development, and will have preliminary clinical evidence in patients to demonstrate the promising activity of the medicine and its potential to address to a significant extent an unmet medical need. In exceptional cases, applicants from the academic sector or SMEs (small and medium sized enterprises) may submit an eligibility request at an earlier stage of development if compelling

non-clinical data in a relevant model provide early evidence of promising activity, and first in man studies indicate adequate exposure for the desired pharmacotherapeutic effects and tolerability.

If a medicine is selected for the PRIME scheme, EMA:

- appoints a rapporteur from the Committee for Medicinal Products for Human Use (CHMP) or from the Committee for Advanced Therapies (CAT) to provide continuous support and to build up knowledge of the medicine in advance of the filing of a marketing authorisation application;
- issues guidance on the applicant's overall development plan and regulatory strategy;
- organises a kick-off meeting with the rapporteur and experts from relevant EMA committees and working groups;
- provides a dedicated EMA contact person; and
- provides scientific advice at key development milestones, involving additional stakeholders, such as health technology assessment bodies and patients, as needed.

Medicines that are selected for the PRIME scheme are also expected to benefit from EMA's accelerated assessment procedure at the time of application for marketing authorization. Where, during the course of development, a medicine no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

Marketing Authorization

To obtain a marketing authorization for a product under EU regulatory systems, an applicant must submit an MAA, either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in EU Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EU. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, applicants must demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan (PIP) covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the European Economic Area (which comprises the 27 Member States of the European Union, together with Norway, Iceland and Liechtenstein). Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, ATMPs and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For those products for which the use of the centralized procedure is not mandatory, applicants may elect to use the centralized procedure where either the product contains a new active substance indicated for the treatment of other diseases or where the applicant can show that the product constitutes a significant therapeutic, scientific or technical innovationor for which a centralized process is in the interest of patients at a European Union level. We anticipate that the centralized procedure will be mandatory for the product candidates we are developing.

Under the centralized procedure, the Committee for Medicinal Products for Human use (or the "CHMP"), which is the EMA's committee that is responsible for human medicines, is responsible for conducting the assessment of whether a medicine meets the required quality, safety and efficacy requirements, and whether the product has a positive benefit/risk profile. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days from the receipt of a valid MAA, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days.

Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the timeframe of 210 days for assessment will be reduced to 150 days (excluding clock stops), but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of EU law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product, the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU Member States and chaired by a non-voting European Commission representative. The European Parliament also has a related "droit de regard". The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

The European Commission may grant a so-called “marketing authorization under exceptional circumstances”. Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a “normal” marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal.

The European Commission may also grant a so-called “conditional marketing authorization” prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the benefit-risk balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

The EU medicines rules expressly permit the EU Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the product candidates we have in development do not make use of embryonic stem cells, it is possible that the national laws in certain EU Member States may prohibit or restrict us from commercializing our product candidates, even if they have been granted an EU marketing authorization.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 70 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, then seek to reach a consensus in relation to the assessment report and related materials within a further 50 days (although there may be clock stops within this period if more information is requested, and such clock stops would extend this time period). If approved at this stage, the application proceeds to the grant procedure at concerned Member States level. If consensus is not reached by the relevant Member States during the initial 120 day period, the application enters a further assessment period. If at the end of that further assessment period a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the EU Member States of the marketing authorization of a medicinal product by the competent authorities of other EU Member States. The holder of a national marketing authorization may submit an application to the competent authority of an EU Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU Member State.

Regulatory Data Protection in the EU

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats the entitlement for medicinal products authorized in accordance with the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During the additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, non-clinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety, and efficacy, including all variations introduced since the marketing authorization was granted, at least nine months before the marketing authorization ceases to be valid.

The European Commission or the competent authorities of the EU Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (in case of centralized procedure) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must also demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to 10 years of market exclusivity in all EU Member States and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. During this market exclusivity period, neither the EMA nor the European Commission or the Member States can accept an application or grant a marketing authorization for the same therapeutic indication in respect of a "similar medicinal product". A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the 10-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation because, for example, the product is sufficiently profitable not to justify market exclusivity.

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the European Union's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.
- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Brexit and the Regulatory Framework in the United Kingdom

In the EU, the General Data Protection Regulation, or GDPR, effective since May 2018, imposes strict regulations and establishes a series of requirements regarding the collection, storage and processing of personally identifiable information on computers or recorded on other electronic media. The GDPR provides for specific regulations requiring certain non-EU based companies doing business in the EU states to provide adequate data privacy protection when receiving personal data from persons in any of the EU member states. We may incur substantial expense in complying with the new obligations imposed by the GDPR and we may be required to make significant changes in our business operations and development, all of which may adversely affect our revenue and our business overall. We could be adversely affected if we fail to comply fully with all of these requirements. Non-compliance with the GDPR can trigger significant fines of up to €20 million or 4% of total worldwide annual turnover, whichever is higher. In addition, the use and disclosure of personal health and other private information are subject to regulation in other jurisdictions in which we do business or expect to do business in the future. Those jurisdictions may attempt to apply such laws extraterritorially or through treaties or other arrangements with European governmental entities. We cannot assure you that our privacy and security policies and practices will be found sufficient to protect us from liability or adverse publicity relating to the privacy and security of personal information.

On June 23, 2016, the UK held a referendum in which a majority of the eligible members of the electorate voted to leave the EU. The UK's withdrawal from the EU is commonly referred to as Brexit. Pursuant to Article 50 of the Treaty on European Union, the UK ceased being a Member State of the EU on January 31, 2020. A transition period began February 1, 2020 and continued until December 31, 2020 during which the UK continued to follow all of the EU's rules and its trading relationship remained the same. 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. The UK, however, is now regarded as a third country under the EU's GDPR which means that transfers of personal data from the EEA to the UK will be restricted unless an appropriate safeguard, as recognised by the EU's GDPR, has been put in place. Although, under the EU-UK Trade Cooperation Agreement it is lawful to transfer personal data between the UK and the EEA for a 6-month period following the end of the transition period, with a view to achieving an adequacy decision from the European Commission during that period. 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 (this means that personal data transfers from the UK to the EEA remain free flowing).

In light of Brexit, it is unclear whether the European Commission, or EC, will grant an adequacy finding to the UK (a finding that the UK privacy legal framework provides an adequate level of privacy protection to EU individuals). Absent an adequacy finding, transfers of personal data from the EU to the UK would be impermissible without adequate safeguards provided for under EC-approved mechanisms, such as current standard contractual clauses or, if approved in the future, an EU – UK privacy shield similar to the current framework in place between the EU and the U.S. The extensive authority of UK intelligence and law enforcement agencies, including to conduct surveillance on personal data flows, could reduce the likelihood that the EC would give the UK an adequacy finding, and reduce the likelihood that the EC would approve an EU – UK privacy shield. Accordingly, we could be exposed to legal risk for any of our EU-UK personal data transfers, including those that involve sensitive data such as patient and genetic data.

Pricing Decisions for Approved Products

In the EU, 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 agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various Member States, and parallel trade, or arbitrage, between low-priced and high-priced Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Human Capital

As of March 1, 2021, we had 118 full-time employees, of which 34 (28%) of our employees have Ph.D. or M.D. degrees and 100 (83%) of our employees are engaged in research and development activities.

Diversity and Inclusion

TCR2 is committed to a culture of diversity, inclusion and belonging. This commitment is reflected in our corporate goals and underpins our social, cultural, and philanthropic initiatives. We focus on diverse recruiting strategies and partner with external organizations that develop and supply diverse talent. In 2020, 76% of our new hires came from underrepresented categories including women, ethnic minorities, LGBTQ+, those with disabilities, and veterans. As of March 1, 2021, approximately 53% of the Company's workforce was female and 44% of the Company's employees in managerial roles were female. As of March 1, 2021, minorities represented approximately 35% of the Company's workforce, of which 23% of our employees in managerial roles were minorities.

Retention, Training and Development

The development, attraction and retention of our employees is a critical success factor for TCR2 and is reflected in our corporate goals. We cultivate a culture of learning and offer formal and informal training and development opportunities for employees at all levels. In 2020 we established our Career Development Model and Guide providing clarity and direction to support the advancement of our employees in our five core competencies: Team Work, Emotional Intelligence, Technical Expertise, Leadership, and Results Orientation. We actively promote from within and continue to fill our team with strong and experienced management talent.

Compensation and Benefits

An important part of attracting and retaining key talent is competitive pay and benefits. To ensure our compensation and benefits programs are competitive, we engage nationally recognized outside compensation and benefits consulting firms to independently evaluate the effectiveness of our programs and to provide benchmarking against our peers within the industry. Our pay for performance philosophy seeks to motivate and reward employees while accomplishing the Company’s short and long-term strategic goals. As part of a robust performance management process, employees are evaluated both on what they accomplished and how they demonstrated our core competencies. Annual salary increases and incentive bonuses are based on merit and include individual and corporate performance factors.

To encourage our employees to think like owners and share in the Company’s success, all employees are granted stock options and can elect to participate in our employee stock purchase plan. All employees are eligible for health insurance, paid and unpaid leaves including paid parental leave, retirement plans with an employer contribution match, life and disability/accident coverage, parking or commuter assistance, an employee assistance program providing mental health, legal and financial health resources, and access to convenient COVID-19 testing.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on May 29, 2015 under the name TCR2, Inc. In November 2016, we changed our name to TCR2 Therapeutics Inc. Our principal executive offices are located at 100 Binney Street, Suite 710, Cambridge, MA 02142, and our telephone number is (617) 949-5200. Our website address is www.tcr2.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report on Form 10-K.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of: (i) the last day of the fiscal year (a) following the fifth anniversary of the completion of the IPO, (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 means the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th, and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Available Information

Our Internet address is www.tcr2.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available through the "Investors" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated herein by reference. In addition, our filings with the SEC may be accessed through the SEC's Interactive Data Electronic Applications system at www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Our code of conduct, corporate governance guidelines and the charters of our Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are available through our website at www.tcr2.com.

Item 1A. Risk Factors

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report on Form 10-K and in other documents that we file with the Securities and Exchange Commission, or SEC, in evaluating the Company and our business. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks facing the Company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impact our business, prospects, financial condition and results of operations.

Risks Related to the Development of Our Product Candidates

Risks Related to Clinical Development

Our approach to the discovery and development of product candidates based on our TRuC-T cell platform represents a novel approach to cancer treatment, which creates significant challenges for us.

Our future success depends on the successful development of our product candidates, which target solid tumors and hematologic malignancies using the complete T cell receptor (TCR) complex without the need for human leukocyte antigen (HLA) matching. Advancing our product candidates based on our innovative TRuC-T cell platform creates significant challenges for us, including:

- educating medical personnel about the administration of TRuC-T cell therapies on a stand-alone basis or in combination with built-in immune and tumor modulators;
- educating medical personnel regarding the potential side effect profile of our product candidates, such as the potential adverse side effects related to cytokine release syndrome (CRS), neurotoxicity or autoimmune or rheumatologic disorders;
- administering chemotherapy to patients in advance of administering our product candidates, which may increase the risk of adverse side effects;
- sourcing clinical and, if licensed, commercial, supplies for the materials used to manufacture and process our product candidates;
- manufacturing viral vectors to deliver TRuC constructs to T cells;
- developing a robust and reliable TRuC-T cell manufacturing process and manufacturing capacity as well as a complete shipment lifecycle and supply chain, including efficiently managing shipment of patient cells from and to clinical sites,

minimizing potential contamination to the cell product during production and effectively scaling manufacturing capacity to meet demand;
- managing costs of inputs and other supplies while scaling production;
- using medicines to manage adverse side effects of our product candidates, which may not adequately control the side effects and/or may have a detrimental impact on the potency of the treatment;
- obtaining and maintaining regulatory approval from the US Food and Drug Administration (FDA) for our product candidates; and
- establishing sales and marketing capabilities upon obtaining any regulatory approval to gain market acceptance of a novel therapy.

In developing our product candidates, we have not exhaustively explored different options in the design of the TRuC construct and in the method for manufacturing TRuC-T cells. We may find our existing TRuC-T cells and manufacturing process may be substantially improved with future design or process changes, necessitating development of new or additional TRuC constructs and further clinical testing and delaying commercial launch of our first products. For example:

- We have made several TRuC constructs and used preclinical studies to select product candidates to advance into clinical trials. The preclinical studies are limited in their ability to predict behavior of our product candidates in patients. As we gain experience working with TRuC constructs, we may decide to select other TRuC constructs for clinical development.
- We have used a lentiviral vector to deliver the TRuC construct to T cells. In the future, we may find that another viral vector or non-viral transfer process offers advantages. Switching from lentiviral to another delivery system would necessitate additional process development and clinical testing and delay the development of existing product candidates.
- The process by which patient cells are converted into a TRuC-T cell has many steps that can influence quality and activity. We have explored a subset of variables and expect to continue to improve and optimize the manufacturing process. Depending upon the nature of the process changes, we may be compelled to perform bridging studies and/or to re-start clinical development, causing delays in time to market and potentially introducing a risk of failure if new processes do not perform as expected.

We are very early in our development efforts. Most of our product candidates are still in preclinical development. 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. Most of our product candidates are still in preclinical development, and gavo-cel, our most advanced product candidate, is in a Phase 1/2 clinical trial. 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. The success of our product candidates will depend on several factors, including the following:

- successful completion of preclinical studies;
- successful initiation and completion of clinical trials;
- successful patient enrollment in and completion of clinical trials;
- receipt and related terms of marketing approvals and licensures from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supply of our product candidates;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- obtaining and maintaining third-party coverage and adequate reimbursement;
- maintaining a continued acceptable safety profile of our products following licensure; and
- effectively competing with other therapies.

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.

We have limited experience as a company in conducting clinical trials.

We have limited experience as a company in conducting clinical trials. Our Phase 1/2 clinical trial for gavo-cel began in 2019 and our Phase 1/2 clinical trial for TC-110 began in 2020. Because of this limited experience, and other factors, we cannot be certain that our planned and ongoing preclinical studies will be completed on time, or that our planned and ongoing clinical trials will begin, enroll sufficient patients, produce data on expected timelines or be completed on expected timelines, if at all. Large-scale clinical trials require significant additional financial and management resources and reliance on third-party clinical investigators, contract

research organizations (CROs) and consultants. Relying on third-party clinical investigators, CROs and consultants may force us to encounter delays that are outside of our control.

Clinical development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future clinical trial results. If our preclinical studies and clinical trials are not sufficient to support regulatory approval of any of our product candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such product candidate.

We cannot be certain that our preclinical study and clinical trial results will be sufficient to support regulatory approval of our product candidates. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Human clinical trials are expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. Failure or delay can occur at any time during the clinical trial process.

We may experience delays in obtaining the FDA's authorization to initiate clinical trials under future INDs, completing ongoing clinical studies of our product candidates due to a variety of factors, including the impact of COVID-19 at our clinical sites, and initiating our planned preclinical studies and clinical trials. Additionally, we cannot be certain that preclinical studies or clinical trials for our product candidates will begin on time, not require redesign, enroll an adequate number of subjects on time, or be completed on schedule, if at all. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;
- delays in obtaining regulatory approval to commence 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 institutional review board (IRB) approval at each clinical trial site;
- recruiting an adequate number of suitable patients to participate in a clinical trial;
- having subjects complete a clinical trial or return for post-treatment follow-up;
- clinical trial sites deviating from clinical trial protocol or dropping out of a clinical trial;
- addressing subject safety concerns that arise during the course of a clinical trial;
- adding a sufficient number of clinical trial sites; or
- obtaining sufficient product supply of product candidate for use in preclinical studies or clinical trials from third-party suppliers.

For example, in February 2019, we received a request from the FDA's Center for Devices and Radiological Health (CDRH) for the submission of an investigational device exemption (IDE) application regarding our use of a commercially available in vitro diagnostic assay for screening mesothelin expression in tumors. The CDRH subsequently determined that we did not need to submit an IDE application, but such a requirement, or other unexpected FDA requests, could lead to future delays of our clinical trials. We may experience numerous adverse or unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon our research efforts for our other product candidates;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of our clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls or be unable to provide us with sufficient product supply to conduct and complete preclinical studies or clinical trials of our product candidates in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the quality of our product candidates or other materials necessary to conduct preclinical studies or clinical trials of our product candidates may be insufficient or inadequate;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- future collaborators may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

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

may be adversely affected and we may incur significant additional costs. In addition, costs to treat patients with relapsed or refractory cancer and to treat potential side effects that may result from our product candidates can be significant. Accordingly, our clinical trial costs are likely to be significantly higher than those for more conventional therapeutic technologies or drug product candidates.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such clinical trials are being conducted, by the Data Safety Monitoring Board (DSMB) for such clinical trial or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial 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 the product candidates, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

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

Our business is highly dependent on our clinical trials for our lead product candidates, gavo-cel and TC-110, and we must complete IND-enabling studies and clinical testing before we can seek regulatory approval and begin commercialization of any of our product candidates. We cannot be certain that we will be able to complete ongoing clinical trials, initiate future planned clinical trials, or advance our product candidates into additional trials, or to successfully develop, or obtain regulatory approval for, or successfully commercialize, any of our product candidates.

Our business depends heavily on our ability to complete clinical development and non-clinical studies of our lead product candidates gavo-cel and TC-110, and our other product candidates, and to obtain regulatory approval of and successfully commercialize these and any future product candidates. There is no guarantee that any of our product candidates will proceed in preclinical or clinical development or achieve regulatory approval. 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 or, if at all.

There is no guarantee that the results obtained in current preclinical studies, our Phase 1/2 clinical trial of gavo-cel, our Phase 1/2 clinical trial of TC-110 or our planned clinical trials will be sufficient to obtain regulatory approval or marketing authorization for such product candidates. The FDA may ultimately decide that the design, number and type of clinical trials, number of patients studied or results of our planned clinical trials for gavo-cel and TC-110, even if positive, are not sufficient for regulatory approval in their respective target indications. Changes in the manufacturing process as we scale-up and optimize our process for manufacturing our product candidates could also delay development or require us to conduct additional clinical trials or non-clinical studies or could lead to different results than achieved with the earlier processes. We may not be able to initiate or complete our clinical trials or announce results from our clinical trials on the timelines we expect. We may experience slower than expected enrollment and randomization of patients in our clinical trials. These types of delays can lead to delays in completion of a trial and announcement of results. There is also the potential for slower than expected clinical site initiation, delays or problems in analyzing data, and the potential need for additional analysis or data or the need to enroll additional patients in any of our clinical trials. We may also encounter delays arising from unexpected adverse events in a trial or other unexpected hurdles or issues in the conduct of any trial. Negative results in the development of our lead product candidates may also impact our ability to obtain regulatory approval for our other product candidates, either at all or within anticipated timeframes because, although other product candidates may target different indications, the underlying technology platform, manufacturing process and development process is the same for all of our product candidates. Accordingly, a failure in any one program may affect the ability to obtain regulatory approval to continue or conduct clinical programs for other product candidates.

In addition, because we have limited financial and personnel resources and are placing significant focus on the development of our lead product candidates, we may forgo or delay pursuit of opportunities with other future product candidates that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and other future product candidates for specific indications may not yield any commercially viable future product candidates. If we do not accurately evaluate the commercial potential or target market for a particular future product candidate, we may relinquish valuable rights to those future product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such future product candidates.

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

Before obtaining regulatory approvals for the commercial sale of our product candidates, including gavo-cel and TC-110, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. We may not be able to demonstrate the efficacy and safety of gavo-cel and TC-110 or any of our other product candidates or any future product candidate at each stage of clinical development or we may encounter issues with any non-clinical studies required for regulatory submissions. Success in preclinical studies or in earlier stage clinical trials may not be repeated or observed in ongoing or future clinical trials involving TRuCs or other product candidates. The results of clinical trials or non-clinical studies of our product candidates at any stage may not support further development or may not be sufficient to obtain regulatory approval.

In 2020 we reported data in our Phase 1/2 clinical trial with gavo-cel for our first eight patients treated on study in dose escalation, including three partial responses according to RECIST 1.1 criteria, and our first ovarian cancer patient having achieved a confirmed partial response. Gavo-cel was also generally well tolerated with none of the first eight patients experiencing neurotoxicity or on-target, off-tumor toxicities and only two patients experiencing gavo-cel-related non-hematologic grade >2 toxicity: one who developed Cytokine Release Syndrome (CRS) grade 3, which was successfully managed with tocilizumab and corticosteroids and a second one who experienced grade 3 CRS and grade 3 pneumonitis that resolved upon administration tocilizumab and corticosteroid therapy. Several weeks after the resolution of the grade 3 CRS and grade 3 pneumonitis, this patient became septic due to a hospital-acquired drug-resistant fungal infection, which was deemed unrelated to gavo-cel by the Safety Review Team (SRT) overseeing the safety of our clinical trial. The SRT declared the grade 3 pneumonitis event as a dose limiting toxicity and recommended the expansion of the dose level 1 cohort from three to six patients. We completed dosing in the expanded cohort in 2020 and have continued treating patients at higher dose levels. While our data in the Phase 1/2 clinical trial has been positive with a manageable safety profile, these results may not be repeated or observed in future cohorts of patients treated in the currently ongoing clinical trial or in future clinical trials and may not be predictive of the results of later-stage clinical trials.

The drug-development process, including preclinical and clinical testing is expensive, can take many years to complete, and may include post-marketing studies and surveillance, which will require the expenditure of substantial resources. The outcome of the drug development process is inherently uncertain. Of the large number of drugs in development in the U.S., only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized. Failure can occur at any time during the preclinical study and clinical trial processes, and, because our product candidates are in an early stage of development, there is a high risk of failure and we may never succeed in developing marketable products. Clinical trials of our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the U.S. and in other countries where we intend to test and, if approved, market any product candidate. Accordingly, even if we have the requisite financial resources, when needed, to continue to fund our development efforts, we cannot assure you that any of our product candidates will be successfully developed or commercialized either in the U.S. or in any country outside the U.S. Even if we gain approval of any of our other product candidates, we may never be able to successfully commercialize the product or to meet our expectations with respect to revenues or profits.

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. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through preclinical studies and clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy 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. Most product candidates that commence preclinical studies and clinical trials are never approved as products.

Any preclinical studies or clinical trials that we may conduct may not demonstrate the safety and efficacy 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 the safety and efficacy 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. There can be significant variability in safety and efficacy 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. Additionally, our preclinical studies comparing our product candidates to chimeric antigen receptor T (CAR-T) cells utilized CAR-T cells that we engineered, rather than the CAR-T cell therapies that are currently approved by the FDA. Although we believe, based on the results we observed in these preclinical studies, that our product candidates have the potential to improve upon the safety and efficacy of currently approved CAR-T cell therapies, these results may not be predictive of the outcome of our future preclinical studies and clinical trials, including any potential preclinical studies and clinical trials that may compare our product candidates to FDA-approved CAR-T cells.

Since the number of patients that we plan to dose in our Phase 1/2 clinical trials is small, the results from these 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.

The number of patients we plan to treat in our clinical trials for gavo-cel and TC-110 is small and the results from these clinical trials, once completed, may be less reliable that results achieved in larger clinical trials. For example, in the Phase 1 portion of our Phase 1/2 clinical trial of gavo-cel, we plan to evaluate the safety profile of gavo-cel and establish the recommended Phase 2 dose. In Phase 2, we intend to treat approximately 50 patients with non-small cell lung cancer (NSCLC), ovarian cancer, malignant pleural/peritoneal mesothelioma and cholangiocarcinoma. The preliminary results of clinical trials with smaller sample sizes, such as our Phase 1/2 clinical trial of gavo-cel, 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 gavo-cel, 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 initial Phase 1/2 clinical trial.

We may not be able to file INDs or IND amendments to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA may not permit us to proceed.

We may not be able to file INDs on the timelines we expect. For example, we may experience manufacturing delays or other delays with IND-enabling studies. In July 2018, a power failure that occurred during our third-party manufacturing run to produce virus for our Phase 1/2 clinical trial of gavo-cel caused us to abandon that manufacturing run and resulted in a month-long delay in the process of manufacturing the requisite virus to support our IND filing for gavo-cel and consequently a delay in the IND filing itself. 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 suspend or terminate clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs.

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, including impacts that have resulted or may result from the COVID-19 pandemic. The timely completion of clinical trials in accordance with their protocols depends on, among other things, our ability to enroll a sufficient number of patients who remain in the clinical trial until its conclusion. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the clinical trial protocol;
- the size of the patient population required for analysis of the clinical trial's primary endpoints;
- the proximity of patients to clinical trial sites;
- the design of the clinical trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patient consents;
- reporting of the preliminary results of any of our clinical trials; and
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before the manufacturing and infusion of our product candidates or clinical trial completion.

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 clinical trials may instead opt to enroll in a clinical trial being conducted by one of our competitors. In addition, patients may be unwilling to participate in our studies because of negative publicity from adverse events in the biotechnology industry or for other reasons. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Moreover, because our product candidates represent a departure from more commonly used methods for cancer treatment, potential patients and their doctors may be inclined to use conventional therapies, such as chemotherapy and hematopoietic stem cell transplantation, rather than enroll patients in any future clinical trial. Additionally, because some of our clinical trials are in patients with relapsed/refractory cancer, the patients are typically in the late stages of their disease and may experience disease progression independent from our product candidates, making them unevaluable for purposes of the clinical trial and requiring additional patient enrollment.

Delays in completing 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 or commencement of these clinical trials and adversely affect our ability to advance the development of our product candidates.

We cannot guarantee that our product candidates will show any functionality in the solid tumor microenvironment.

There are no approved CAR-T or engineered TCR-T cell immunotherapies for solid tumors. We believe our TruC-T cell product candidates may be effective against solid tumors. While we plan to develop product candidates for use in solid tumors, including gavo-cel, we cannot guarantee that our product candidates will show any functionality in the solid tumor microenvironment. The cellular environment in which solid tumor cells thrive is generally hostile to T cells due to factors such as the presence of immunosuppressive cells, humoral factors and limited access to nutrients. Our TRuC-T cell-based product candidates may not be able to access the solid tumor, and even if they do, they may not be able to exert anti-tumor effects in a hostile tumor microenvironment. In addition, the safety profile of our product candidates may differ in a solid tumor setting. As a result, our product candidates may not demonstrate potency in solid tumors. If we are unable to make our product candidates function in solid tumors, our development plans and business may be significantly harmed.

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

Undesirable side effects caused by our product candidates could cause us or regulatory authorities, including IRBs, to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. 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. Because of our planned dose escalation design for our clinical trials, 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, which may stem from our product candidates specifically or may be due to an illness from which the clinical trial subject is suffering. In 2020 we reported data in our Phase 1/2 clinical trial with gavo-cel for our first eight patients treated on study in dose escalation, including three partial responses according to RECIST 1.1 criteria, and our first ovarian cancer patient having achieved a confirmed partial response. Gavo-cel was also generally well tolerated with none of the first eight patients experiencing neurotoxicity or on-target, off-tumor toxicities and only two patients experiencing gavo-cel-related non-hematologic grade >2 toxicity: one who developed Cytokine Release Syndrome (CRS) grade 3, which was successfully managed with tocilizumab and corticosteroids and a second one who experienced grade 3 CRS and grade 3 pneumonitis that resolved upon administration tocilizumab and corticosteroid therapy. Several weeks after the resolution of the grade 3 CRS and grade 3 pneumonitis, this patient became septic due to a hospital-acquired drug-resistant fungal infection, which was deemed unrelated to gavo-cel by the Safety Review Team (SRT) overseeing the safety of our clinical trial. The SRT declared the grade 3 pneumonitis event as a dose limiting toxicity and recommended the expansion of the dose level 1 cohort from three to six patients. We completed dosing in the expanded cohort in 2020 and have continued treating patients at higher dose levels. While our data in the Phase 1/2 clinical trial has been positive with a manageable safety profile, these results may not be repeated or observed in future cohorts of patients treated in the currently ongoing clinical trial or in future clinical trials and may not be predictive of the results of later-stage clinical trials.

Autoimmunity may occur after TRuC-T cell treatment. TRuC-T cells are generated from a patient's own T cells isolated from their peripheral blood. There is a theoretical risk that this process will expand a patient's own T cell that has autoreactivity, or that may recognize healthy cells, and upon re-infusion may trigger an autoimmune reaction resulting in damage to normal tissues and potentially even death. Autoimmune reaction triggered by an interaction between a patient's naturally occurring antibodies and engineered T cells is a theoretical safety risk of product candidates we develop using our TRuC-T cell platform. If a patient's self-generated antibodies were directed to a target expressed on the surface of cells in normal tissue (autoantibodies), engineered T cells would be directed to attack these same tissues, potentially resulting in off-tumor effects. These autoantibodies may be present whether or not the patient has an active autoimmune disease. In our clinical testing, we plan to take steps to minimize the likelihood that this occurs, for example by excluding patients with a history of severe autoimmune disease from our trials. There is no guarantee, however, that we will not observe autoimmune reactions in the future and no guarantee that if we do, that we will be able to implement interventions to address the risk.

Immunogenicity, which is the reaction between a patient's immune system and a foreign protein outside of the autoimmune context, is an additional theoretical safety risk of product candidates we develop using our TRuC-T cell platform. Patients' immune systems may recognize the TRuC construct on the TRuC-T cell as a foreign protein and fight against it, potentially rendering it ineffective, or even provoking an allergic/anaphylactoid response or other adverse side effects. The immunogenic potential of novel therapeutics like TRuC-T cells is difficult to predict. There is no guarantee that we will not observe immunogenic reactions in the future and no guarantee that if we do, that we will be able to implement interventions to address the risk.

If unacceptable toxicities arise in the development of our product candidates, we could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities, or local regulatory authorities such as IRBs, could order us to cease clinical trials. Competent national health 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 patients to complete the clinical 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 our product candidates to understand the side effect profile of our product candidates for both our planned clinical trials and upon any commercialization of any 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 significantly harm our business, financial condition and prospects.

Our product candidates may target healthy cells expressing target antigens leading to potentially fatal adverse effects.

Our product candidates target specific antigens that are also expressed on healthy cells. For example, our lead product candidate, gavo-cel, targets mesothelin, an antigen commonly found on mesotheliomas, ovarian cancers, and NSCLC, as well in healthy cells that line the pleura, pericardium and peritoneum. TC-110 targets CD19, which is overexpressed in several cancers including B-cell leukemias and lymphomas, but is also expressed by normal B-cells. Our product candidates may target healthy cells, leading to serious and potentially fatal adverse effects. In our Phase 1/2 clinical trial of gavo-cel, we are using a dose escalation model to closely monitor the effect of gavo-cel on vital organs and other potential side effects. In clinical testing of TC-110, we also plan to closely monitor the effect of TC-110 on normal B-cells that express CD19 and for other side effects. Even though we intend to closely monitor the side effects of our product candidates in both preclinical studies and clinical trials, we cannot guarantee that products will not target and kill healthy cells.

Our product candidates may have serious and potentially fatal cross-reactivity to other peptides or protein sequences within the body.

Our product candidates may recognize and bind to a peptide unrelated to the target antigen to which it is designed to bind. If this peptide is expressed within normal tissues, our product candidates may target and kill the normal tissue in a patient, leading to serious and potentially fatal adverse effects. Detection of any cross-reactivity may halt or delay any ongoing clinical trials for any TRuC-T cell based product candidate and prevent or delay regulatory approval. Unknown cross-reactivity of the TRuC-T cell binding domain to related proteins could also occur. We have also developed a preclinical screening process to identify cross-reactivity of the TRuC-T cell binders. Any cross-reactivity 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.

Our product candidates rely on the use of protein binding domains, or binders, to target specific cancers, which we may develop or which may be developed by third parties. We are limited in our ability to apply our product candidates to a wider range of potential target cancers by our ability to develop, partner for or acquire these binders on commercially reasonable terms.

TRuC-T cell therapies require the use of antigen-specific protein binding domains, or binders, which guide the TRuC-T cells and bind to the antigens on the surface of a tumor to target specific types of cancers. Our ability to develop and commercialize our product candidates will depend on our ability to develop these binders or partner for such binders on commercially reasonable terms for use in clinical trials as well as the availability of such binders for use in commercialized products, if licensed. For example, we have a non-exclusive license for the mesothelin binder incorporated into the TRuC construct for gavo-cel from Harpoon Therapeutics, Inc. (Harpoon). However, we cannot be certain that our Harpoon license or potential future collaborations will provide us with a steady supply of binders that we can utilize in combination with the TRuC construct to develop future product candidates. If we are unable to enter into such collaborations on commercially reasonable terms or fail to realize the benefits of any such collaboration, we may be limited to using antibody fragments that we are able to independently develop which may limit the ability of our product candidates to target and kill cancer cells.

The failure to enter into a successful collaboration or to develop our own binders may delay our development timelines, increase our costs and jeopardize our ability to develop future product candidates as a commercially viable drug, which could result in delays in product development and harm our business.

We may not be successful in our efforts to identify or discover additional product candidates.

The success of our business depends primarily upon our ability to identify, develop and commercialize products based on our TRuC T-cell platform. Our research programs may fail to identify other potential product candidates for clinical development for a number of reasons. We may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be

unsuccessful. If any of these events occur, we may be forced to abandon our research, development or commercialization efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Risks Related to Manufacturing

Manufacturing and administering our product candidates are complex and 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 TRuC-T cells for clinical trials or for commercial purposes could be delayed or stopped.

The process of manufacturing and administering our product candidates is complex and highly regulated. The manufacture of our product candidates involves complex processes, including the manufacture of a lentiviral delivery vector containing the genetic information for our TRuC construct and manufacturing T cells containing the TRuC construct for the final product candidates. More specifically, the manufacture of our product candidates includes harvesting white blood cells from the patient, isolating certain T cells from the white blood cells, 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. As a result of the complexities entailed in this process, our manufacturing and supply costs are likely to be higher than those at more traditional manufacturing processes and the manufacturing process is less reliable and more difficult to reproduce. Additionally, the number of facilities that are capable of harvesting patients' cells for the manufacture of our product candidates and other autologous cell therapy products and product candidates is limited. As the number of autologous cell therapy products and product candidates increases, the limited number of facilities capable of harvesting patients' cells could result in delays in the manufacture and administration of our product candidates and/or require us to prioritize among our clinical programs, potentially resulting in clinical trial delays.

We rely on third parties for the manufacture of our lentiviral vectors and our product candidates. These third-party manufacturers may incorporate their own proprietary processes into our lentiviral vector and product candidate manufacturing processes. We have limited control and oversight of a third party's proprietary process, and a third party may elect to modify its process without our consent or knowledge. These modifications could negatively impact our manufacturing, including product loss or failure that requires additional manufacturing runs or a change in manufacturer, both of which could significantly increase the cost of and significantly delay the manufacture of our product candidates. In addition these third parties may have limited manufacturing capacity, causing delays in planned manufacturing runs, and limiting our ability to manufacture lentiviral vector and our product candidates as needed, resulting in delays for IND filings, clinical trials and non-clinical studies.

Our manufacturing process is and will be susceptible to product loss or failure due to logistical issues, including manufacturing issues associated with the differences in patients' white blood cells, interruptions in the manufacturing process, contamination, equipment or reagent failure, power failures, supplier error and variability in patient characteristics. For example, in July 2018, a power failure that occurred during a manufacturing run to produce virus for our Phase 1/2 clinical trial of gavo-cel caused us to abandon that run, and resulted in a month-long delay in the process of manufacturing the requisite virus to support our IND filing for gavo-cel and consequently a delay in the IND filing itself. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If for any reason we lose a patient's white blood cells, or such material gets contaminated or processing steps fail at any point, the manufacturing process of the TRuC-T cells for that patient will need to be restarted and the resulting delay may adversely affect that patient's outcome. If microbial, viral or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made or administered, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.

As our product candidates progress through preclinical studies and clinical trials towards potential licensure and commercialization, it is expected that various aspects of the manufacturing and administration process will be altered in an effort to optimize processes and results. We have already identified some improvements to our manufacturing and administration processes, but these changes may not achieve the intended objectives, and could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials. In addition, such changes may require amendments to be made to regulatory applications which may further delay the timeframes under which modified manufacturing processes can be used for any of our product candidates.

Developing a commercially viable process 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. In addition, changes to our manufacturing process may also require further review and approval by the FDA, leading to delays in our clinical trials. Competitors have had difficulty reliably producing 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 approved. 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.

We do not have our own clinical-scale manufacturing facility and are currently reliant on a limited number of manufacturers for our lentiviral vector and a single manufacturer to provide our needs for producing our TRuC-T cell product candidates. We are in the process of adding manufacturing capacity to support larger clinical trials for our product candidates and have occupied a GMP manufacturing suite at Catapult in Stevenage, United Kingdom. We plan to pursue additional manufacturing capacity in the United States and in Europe to meet our future demands and may build our own manufacturing capabilities to meet the patient demand for our product candidates. These third-party manufacturing providers may not be able to provide adequate resources or consistent capacity to meet our clinical trial or commercial needs.

We rely on third parties to manufacture our product candidates for our clinical trials.

We rely on third parties for the manufacture of our lentiviral vectors and our product candidates. We do not currently own any facility that may be used as our clinical scale manufacturing facility for our product candidates or lentiviral vector and we expect to rely on outside vendors to meet these manufacturing needs. Our GMP manufacturing suite at the Cell and Gene Therapy Catapult Limited center in Stevenage, United Kingdom (Catapult) is now operational, and, subject to the impact of COVID-19, we expect to obtain MHRA certification in the middle of 2021. We have also partnered with Elevate Bio, LLC for access to Elevate Bio BaseCamp, its 140,000 square foot, world-class cell and gene therapy manufacturing facility based in Waltham, MA. The BaseCamp partnership enables us to establish additional manufacturing capacity and technical capabilities in the United States, in addition to our existing Stevenage, United Kingdom, manufacturing facility. However, even once we are producing clinical trial material at Catapult and at ElevateBio, we will still continue to rely on third party manufacturers to meet our clinical trial demands. We have not yet caused any product candidates to be manufactured or processed on a commercial scale and may not be able to do so for any of our product candidates. We plan to make changes as we work to optimize the manufacturing process. For example, we may switch or be required to switch from research-grade materials to commercial-grade materials in order to get regulatory approval of our product candidates. We cannot be sure that even minor changes in the process will result in therapies that are safe and effective and licensed for commercial sale.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA, as part of our BLA, or other foreign regulatory authorities following inspections by the FDA or other foreign regulatory authorities. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMPs and any other regulatory requirements of the FDA or other regulatory authorities for the manufacture of our product candidates. We have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority finds deficiencies with or does not approve these facilities for the manufacture of our product candidates or if it finds deficiencies or withdraws any approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates.

We plan to 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 and the use of third-party manufacturing suites, which will be costly, time-consuming, and which may not be successful.

We are in the process of adding manufacturing capacity with Catapult's GMP manufacturing center and through our partnership with ElevateBio for our larger clinical trials. We may also establish our own commercial manufacturing facility. This should mitigate our reliance on third-party vendors for the manufacture of TRuC-T cells and ensure we can effectively manage our supply chain, quality, manufacturing costs and other associated production areas. Our manufacturing suite at Catapult is now operational, and we expect to obtain MHRA certification in the middle of 2021. We anticipate that our suite at Catapult and the partnership with ElevateBio will significantly increase our total manufacturing capacity. Ability to use our product candidates manufactured in our suite at Catapult for our clinical trials will depend on, among other factors, receiving appropriate approvals and clearance from the UK's Medicines and Healthcare Products Regulatory Agency (MHRA), and the successful recruitment and training of appropriate personnel to support full operation of the manufacturing suite. While we are relying on consultants and other resources with MHRA licensing experience, as a company, we have no prior experience in gaining MHRA approval for a manufacturing facility, and our approval is dependent in part on the timely support, actions and compliance of Catapult, as well, which we are not able to control. Any delay in the MHRA approval or our ability to attract and train personnel may delay the manufacture of clinical trial material in our suite at Catapult, causing us to continue to reply on third-party manufacturing. In addition, the Cell and Gene Therapy Catapult facility contains suites for multiple companies. All companies in the facility must follow proper GMP guidelines in order to maintain the facility's compliance. Failure of another company to properly follow GMP guidelines could affect the facility's GMP compliance and our ability to manufacture our product candidates for our clinical trials at the Cell and Gene Therapy Catapult facility.

The establishment of our own commercial manufacturing facility would be a costly and time-consuming process that we expect to require additional capital to fund and take several years before becoming operational. We have no experience as a company in setting up, building or managing a manufacturing facility or manufacturing suite, and may never be successful in developing our own

manufacturing suite, manufacturing facility or manufacturing capability. We will need to hire additional personnel to manage our operations and facilities and develop the necessary infrastructure to continue the research and development, and eventual commercialization, if approved, of our product candidates. If we fail to recruit the required personnel and generally manage our growth effectively or fail to select the correct location, the development and production of our product candidates could be curtailed or delayed. Even if we are successful in establishing a manufacturing suite or manufacturing facility, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, labor shortages, natural disasters, power failures and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

In addition, the FDA, the European Medicines Agency (EMA) and other foreign regulatory authorities may require us to submit samples of any lot of any licensed product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other foreign regulatory authorities may require that we not distribute a lot until the relevant agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects. Problems in our manufacturing process could restrict our ability to meet market demand for our products. If we establish our own commercial manufacturing facility in the United States, 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.

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

Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs.

We may have difficulty validating our manufacturing process as we manufacture TRuC-T cells from an increasingly diverse patient population for our clinical trials.

During our development of the manufacturing process, our TRuC-T cells have demonstrated consistency from lot to lot and from donor to donor. However, our sample size is small and the starting material is from healthy donors. Once we have experience with working with white blood cells taken from our patient population, we may encounter unforeseen difficulties due to starting with material from donors who are not healthy, including challenges inherent in harvesting white blood cells from unhealthy patients.

Although we believe our current manufacturing process is scalable for commercialization, we may encounter challenges in validating our process due to the heterogeneity of the product starting material. However, we anticipate that during the early phases of our clinical trials we will be able to adapt our process to account for these differences resulting in a more robust process. We cannot guarantee that any other issues relating to the heterogeneity of the starting material will not impact our ability to commercially manufacturing our product candidates.

The viral vectors used to manufacture our TRuC-T cells may incorrectly modify the genetic material of a patient's T cells, potentially triggering the development of a new cancer or other adverse events.

Our TRuC-T cells are manufactured by using a viral vector to insert genetic information encoding the TRuC construct into the patient's T cells. The TRuC construct is then integrated into the natural TCR complex and transported to the surface of the patient's T cells. Because the viral vector modifies the genetic information of the T cell, there is a theoretical risk that modification will occur in the wrong place in the T cell's genetic code, leading to vector-related insertional oncogenesis, and causing the T cell to become cancerous. If the cancerous T cell is then administered to the patient with the TRuC-T cells, the cancerous T cell could trigger the development of a new cancer in the patient. We use lentiviral vectors to insert genetic information into T cells, which we believe have a lower risk of insertional oncogenesis as opposed to other types of viral vectors. However, the risk of insertional oncogenesis remains a concern for gene therapy and we cannot assure that it will not occur in any of our ongoing or planned preclinical studies or clinical trials. There is also the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of vectors used to carry the genetic material. The FDA has stated that lentiviral vectors possess characteristics that may pose high risks of delayed adverse events. If any such adverse events occur, further advancement of our preclinical studies or clinical trials could be halted or delayed, which would have a material adverse effect on our business and operations.

Risks Related to Commercialization

The market opportunities for our product candidates may be relatively small as it will be limited to those patients who are ineligible for or have failed prior treatments and our estimates of the prevalence of our target patient populations may be inaccurate.

Cancer therapies are sometimes characterized as first line, second line, or third line, and the FDA often approves new therapies initially only for a particular line of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, usually chemotherapy, antibody drugs, tumor-targeted small molecules, hormone therapy, radiation therapy, surgery, or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules, or a combination of these. Third line therapies can include hematopoietic stem cell transplantation in certain cancers, chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery and new technologies. We expect to initially seek approval of our product candidates in most instances at least as a second or third line therapy, for use in patients with relapsed or refractory metastatic cancer. Subsequently, for those product candidates that we believe prove to be sufficiently safe and beneficial, if any, we would expect to seek approval as a second line therapy and potentially as a first line therapy, but there is no guarantee that our product candidates, even if licensed as a second or third or subsequent line of therapy, would be licensed for an earlier line of therapy, and, prior to any such approvals, we may have to conduct additional clinical trials. Consequently, the potentially addressable patient population for our product candidates may be extremely limited or may not be amenable to treatment with our product candidates.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive a particular line 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 therapies may change the estimated incidence or prevalence of the cancers that we are targeting. Consequently, even if our product candidates are approved for a second or third line of therapy, the number of patients that may be eligible for treatment with our product candidates may turn out to be much lower than expected.

We face significant competition, and our operating results will suffer if we fail to compete effectively.

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our competitors may be able to develop other products or drugs that are able to achieve similar or better results. Our potential competitors include larger biotechnology and pharmaceutical companies with greater resources than us, academic institutions, governmental agencies, public and private research institutions and early stage or smaller companies. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff, experienced marketing and manufacturing organizations and well-established sales forces. In addition, many of these competitors are active in seeking patent protection and licensing arrangements in anticipation of collecting royalties for use of technology that they have developed. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products. We believe the key competitive factors that will affect the development and commercial success of our product candidates are safety, potency, purity, tolerability, reliability, convenience of use, price and reimbursement.

The market opportunity in oncology has led to a number of collaborations GlaxoSmithKline plc (GlaxoSmithKline)/Adaptimmune Therapeutics PLC (Adaptimmune), Janssen Biotech, Inc. (Janssen)/ Nanjing Legend Pharmaceutical & Chemical Co., Ltd (Legend), bluebird bio, Inc. (bluebird)/ Regeneron Pharmaceuticals Inc. (Regeneron) and bluebird/Gritstone Oncology, Inc.) and major acquisitions (Gilead Sciences, Inc. (Gilead)/Kite Pharma Inc. (Kite), Bristol Myers Squibb Co (BMS)/Celgene Corporation (Celgene)/Juno Therapeutics, Inc. (Juno)) among companies focused on cellular cancer therapies. Specifically, we face significant competition from companies developing chimeric antigen receptor (CAR-T), TCR, and T cell directed bispecific antibody technologies. For our product candidates targeting mesothelin-expressing solid tumors, antibody-based approaches are being pursued by F. Hoffmann-La Roche Ltd, Bayer AG, Bristol-Myers Squibb Company, Selecta Biosciences, Inc., Novimmune SA, Harpoon Therapeutics, Inc., Amgen Inc., Abbvie Inc., and Morphotek, Inc., among others, and cell therapies are being pursued Tmunity Therapeutics, Inc., Atara Biotherapeutics, Inc., Memorial Sloan Kettering Cancer Center, the National Institutes of Health Clinical Center, Maxcyte, Inc., Legend Biotech Corp, Gracell Biotechnology Inc., CARISMA Therapeutics Inc., Refuge Biotechnologies, Inc., Adaptimmune Therapeutics PLC, Kiromic Biopharma, Inc. and and several Chinese academic institutions. For our product candidates targeting CD-19 expressing hematological malignancies, recent regulatory approvals of Gilead's, Novartis' and Bristol-Meyers Squibb's CAR-T cell therapies have led a number of companies to increase their research and development efforts in the cell therapeutics field, including Janssen through its collaboration with Legend, as well as the entry into the field by

many other companies. In addition to these CAR-T cell therapies, many companies are developing enhanced cell therapies, which may compete with TC-110. These include Cellectis S.A./Allogene Therapeutics, Inc., Mustang Bio, Inc., Autolus Therapeutics plc, Crispr Therapeutics AG, Precision BioSciences, Inc., Sana Biotechnology, Inc., Eureka Therapeutics, Inc., Triumvira Immunologics, Inc., Poseida Therapeutics, Inc., Takeda Pharmaceutical Co Ltd, Fate Therapeutics Inc. and Miltenyi Biotec GmbH, among others. Companies such as F. Hoffmann-La Roche Ltd, Genmab A/S, Amgen Inc., Xencor Inc., Regeneron, ADC Therapeutics SA, MorphoSys AG, IGM Biosciences, Inc., Forty Seven, Inc., and others are pursuing antibody based approaches. Even if we obtain regulatory approval of our product candidates, the availability and price of our competitors' 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. For additional information regarding our competition, see "Business—Competition."

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

The use of engineered T cells as a potential cancer treatment is a recent development and may not become broadly accepted by physicians, patients, hospitals, cancer treatment centers and others in the medical community. Various 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, cancer 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;
- our ability to demonstrate the advantages of our product candidates over other engineered TCR-T cell and CAR-T cell therapies;
- the prevalence and severity of any side effects;
- the prevalence and severity of any side effects for other adoptive cell therapies, engineered TCR-T cell and CAR-T cell products and public perception of other adoptive cell therapies, engineered TCR-T cell and CAR-T cell products;
- 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 adequate coverage, reimbursement and pricing by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage 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.

In addition, although we are not utilizing embryonic stem cells or replication competent vectors, adverse publicity due to the ethical and social controversies surrounding the therapeutic use of such technologies, and reported side effects from any clinical trials using these technologies or the failure of such clinical trials to demonstrate that these therapies are safe and effective may limit market acceptance of our product candidates. If our product candidates are licensed but fail to achieve market acceptance among physicians, patients, hospitals, cancer treatment centers or others in the medical community, we will not be able to generate significant revenue.

In addition, although our product candidates differ in certain ways from other engineered TCR-T cell and CAR-T cell approaches, serious adverse events or deaths in other clinical trials involving engineered TCR, CAR-T or other T cell products or with our use of licensed engineered TCR-T cell or CAR-T cell products, even if not ultimately attributable to our product or product candidates, could result in increased government regulation, unfavorable public perception and publicity, potential regulatory delays in the testing or licensing of our product candidates, stricter labeling requirements for those product candidates that are licensed, and a decrease in demand for any such product candidates.

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 Our Reliance On Third Parties

Third Party Risks Related to Our Product Development

We plan to rely on third parties to conduct our clinical trials. If these third parties do not properly and 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 plan to utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs and strategic partners to conduct our preclinical studies and clinical trials under agreements with us. We expect to have to negotiate budgets and contracts with CROs, trial sites and CMOs which may result in delays to our development timelines and increased costs. We will rely heavily on these third parties over the course of our clinical trials, and we control only certain aspects of their activities. As a result, we will have less direct control over the conduct, timing and completion of these clinical trials and the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities 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 regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP regulations. In addition, our clinical trials must be conducted with biologic product produced under cGMP regulations, including cGTP regulations, and will require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our clinical trials are not and 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, clinical and non-clinical product candidates. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, 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.

Switching or adding third parties to conduct our clinical trials involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines.

If or until we develop our own manufacturing facility, we expect to rely on the use of manufacturing suites in third-party GMP facilities or third parties to manufacture our product candidates. Our business could be harmed if we are unable to use third-party manufacturing suites or if the third-party manufacturers fail to provide us with sufficient quantities of our product candidates or fail to do so at acceptable quality levels or prices.

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and must currently rely on outside vendors to manufacture and process our product candidates, which is and will need to be done on a patient-by-patient basis. We are in the process of adding manufacturing capacity at a suite in Catapult's GMP manufacturing center, but staffing, training, and regulatory approval of the manufacturing suite may be delayed and the suite may never become operational. We have not yet caused our product candidates to be manufactured or processed on a commercial scale and may not be able to do so for any of our product candidates.

Although in the future we plan to build our own manufacturing facility, we also intend to use the manufacturing suite at Catapult, ElevateBio BaseCamp and other third parties as part of our manufacturing process and may, in any event, never be successful in developing our own manufacturing facility. 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 must inspect any manufacturers for current cGMP and cGTP compliance as part of our marketing application;
- a new manufacturer would have to be educated in, or develop substantially equivalent processes for, the production of our product candidates, which can take several months or more, and we will need to demonstrate to regulatory authorities that clinical trial product manufactured at a new supplier is comparable to clinical trial product being produced by current manufacturers;
- our manufacturers may have little or no experience with autologous cell products, which are products made from a patient's own cells, and therefore may require a significant amount of support from us in order to implement and maintain the infrastructure and processes required to manufacture our product candidates;
- our third-party manufacturers might be unable to timely manufacture our product candidates 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 and other logistical support requirements appropriately, affecting quality of our product and requiring additional runs to remanufacture product that is suitable for use in clinical trials;
- our future contract manufacturers may not perform as agreed, may not devote sufficient resources to our product candidates 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 products, if any;
- manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMP, cGTP and other government regulations and corresponding foreign standards. 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 agreements with us;
- raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available or may not be suitable or acceptable for use due to material or component defects;
- our contract manufacturers and critical reagent suppliers may be subject to inclement weather, pandemics and natural or man-made disasters; and
- our contract manufacturers may have unacceptable or inconsistent product quality success rates and yields, and we have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel.

Each of these risks could delay or prevent the completion of our clinical trials or the approval of any of our product candidates by the FDA, result in higher costs or adversely impact commercialization of our product candidates. In addition, we will rely on third parties to perform certain specification 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 and the FDA could place significant restrictions on our company until deficiencies are remedied.

The manufacture of biological drug products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of biologic products often encounter difficulties in production, particularly in scaling up or out, validating the production process and assuring high reliability of the manufacturing process (including the absence of contamination). These problems include logistics and shipping, difficulties with production costs and yields, quality control, including stability of the product, product testing, operator error and availability of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if contaminants are discovered in our supply of our product candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any stability failures or other issues relating to the manufacture of our product candidates will not occur in the future.

We may fail to manage the logistics of collecting and shipping patient material to the manufacturing site and shipping the product candidate back to the patient. Logistical and shipment delays and problems caused by us, our vendors or other factors not in our control, such as weather, could prevent or delay the delivery of product candidates to patients. Additionally, we have to maintain a complex chain of identity and chain of custody with respect to patient material as it moves to the manufacturing facility, through the manufacturing process and back to the patient. Failure to maintain chain of identity and chain of custody could result in patient death, loss of product or regulatory action.

Our manufacturing process needs to comply with FDA and MHRA regulations relating to the quality and reliability of such processes. Any failure to comply with relevant regulations could result in delays in or termination of our clinical programs and suspension or withdrawal of any regulatory approvals.

In order to commercially produce our products either at our own facility or at a third party's facility, we will need to comply with the FDA's cGMP regulations and guidelines and the MHRA's regulations and guidelines, including cGTPs. We may encounter

difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We are subject to inspections by the FDA, MHRA and comparable foreign regulatory authorities to confirm compliance with applicable regulatory requirements. Our manufacturing operations in the UK are also dependent on meeting MHRA regulations and results from regular facility inspections. Any failure to follow cGMP, cGTP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, fill-finish, packaging, or storage of our TRuC-T cells as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our TRuC-T cell programs, including leading to significant delays in the availability of our TRuC-T cells for our clinical trials or the termination of or suspension of a clinical trial, or the delay or prevention of a filing or approval of marketing applications for our TRuC-T cell product candidates. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our TRuC-T cell product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business.

If our third-party manufacturers use hazardous and biological 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, by our third-party manufacturers. Our manufacturers 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 our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we 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.

Risks Related to Third Party Agreements

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

Further, collaborations involving our product candidates are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization of our product candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;

- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our product candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

As a result, if we enter into additional collaboration agreements and strategic partnerships or license our product candidates, 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, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Any delays in entering into new collaborations or strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

Our product candidates rely on the availability of specialty raw materials, which may not be available to us on acceptable terms or at all.

Our product candidates require many specialty raw materials, some of which are manufactured by small companies with limited resources and experience to support a commercial product. In addition, those suppliers normally support blood-based hospital businesses and 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 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 of our raw materials are currently available from a single supplier, or a small number of suppliers. The type of cell culture media and cryopreservation buffer that we currently use in our manufacturing process for the TRuC-T cells for gavo-cel and TC-110 are each only available from a single supplier. In addition, the cell processing equipment and tubing that we use in our current manufacturing process is only available from a single supplier. We also use certain biologic materials, including certain activating antibodies, that are available from multiple suppliers, but each version may perform differently, requiring us to characterize them and potentially modify some of our protocols if we change 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. Accordingly, if we no longer have access to these suppliers, we may experience delays in our clinical or commercial manufacturing which could harm our business or results of operations.

Risks Related to Our Financial Condition and Capital Requirements

Risks Related to Operating History

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.

We are a clinical-stage immunotherapy company with a limited operating history. We commenced operations in May 2015, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, filing patent applications, identifying potential product candidates, undertaking preclinical studies, establishing arrangements with third parties for the manufacture of initial quantities of our product candidates and component materials and initiating and conducting our first clinical trials. We have two product candidates in Phase 1/2 clinical trials and our other product candidates are still in preclinical development. We have not yet demonstrated our ability to successfully conduct or complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

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

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We have incurred significant losses since inception, and we expect to incur losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future.

Investment in biopharmaceutical product development is a highly speculative undertaking and 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 are still in the early stages of development of our product candidates. We have no products licensed for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. We have financed our operations primarily through private placements of our preferred stock, our initial public offering and subsequent public offerings.

We have incurred significant net losses in each period since our inception in May 2015. For the year to date ended December 31, 2020, we incurred a net loss of $67.1 million. As of December 31, 2020, we had an accumulated deficit of $249.7 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase substantially if and as we:

- conduct clinical trials and preclinical studies and clinical trials for our current and future product candidates based on our TRuC-T cell platform;
- continue our research and development efforts and submit IND applications for our lead product candidates;
- establish and expand our manufacturing capabilities for both clinical and commercial supplies of our product candidates;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- build commercial infrastructure to support sales and marketing for our product candidates;
- expand, maintain and protect our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel; and
- continue to operate as a public company.

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 not generated any revenue from our product candidates and may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from any of our product candidates. We do not expect to generate significant revenue unless or until we successfully complete clinical development and obtain regulatory approval of, and then successfully commercialize, at least one of our product candidates. Other than gavo-cel and TC-110, all of our product candidates are in the preclinical stages of development and 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. gavo-cel, our most advanced mono TRuC-T cell product candidate targeting mesothelin-positive solid tumors, is in the early stages of a Phase 1/2 clinical trial and will require additional 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. Many of our TRuC-T cell product candidates are in early preclinical stages. We are in the early stages of our clinical trial for gavo-cel and we have not yet administered any of our other product candidates 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 contractors;
- our ability to complete IND-enabling studies and successfully submit INDs or comparable applications;
- whether we are required by the FDA or similar foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our product candidates or any future product candidates;
- our ability to demonstrate to the satisfaction of the FDA and similar foreign regulatory authorities the safety, potency, purity, of which potency and purity the FDA interprets to mean effectiveness, 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 timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities;
- the willingness of physicians, operators of clinics and patients to utilize or adopt any of product candidates or future product candidates to treat solid tumors and hematological malignancies;
- 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 current good manufacturing practices (cGMP);
- our ability to successfully develop a commercial strategy and thereafter commercialize our product candidates or any future product candidates in the United States and internationally, if licensed for marketing, reimbursement, sale and distribution in such countries and territories, 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.

Risks Related to Raising Additional Capital

If we fail to obtain additional financing, we may be unable to continue our research and product development programs.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts (including net proceeds from public offerings of our common stock) to continue the clinical development of our product candidates, including our Phase 1/2 clinical trial of gavo-cel and ongoing and planned IND-enabling studies for our other product candidates. If licensed, we will require significant additional amounts in order to launch and commercialize our product candidates.

In February 2019, we completed our initial public offering (IPO) raising gross proceeds of approximately $86.3 million, inclusive of the exercise of the underwriters' overallotment option. On July 31, 2020, we completed a stock offering raising gross proceeds of approximately $142.6 million. On January 22, 2021, we completed a stock offering raising gross proceeds of approximately $140 million. As of December 31, 2020 we had cash, cash equivalents and short-term investments of approximately $228.0 million. Our existing cash, cash equivalents and short-term investments may not be sufficient to fund all of our efforts that we plan to undertake.

We believe that our existing cash, cash equivalents and investments, including our net proceeds from the IPO and secondary offering, will be sufficient to fund our operations at least into 2024. 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. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue our research and development initiatives. 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.

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

Raising additional capital may cause dilution to our 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.

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

The current outbreak of novel coronavirus, or COVID-19, has caused, and could continue to cause, severe disruptions in the U.S., regional and global economies and could seriously harm our development efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.

Public health pandemics or outbreaks could adversely impact our business. In December 2019, a novel strain of coronavirus (COVID-19) emerged in Wuhan, Hubei Province, China and has since spread to several other countries, including the United States and European countries, with infections and deaths reported globally. To date, the COVID-19 pandemic has caused widespread disruptions to the U.S. and global economy and has contributed to significant volatility and negative pressure in financial markets. The global impact of the outbreak is continually evolving and, as additional cases of the virus are identified, many countries, including the U.S., have reacted by instituting quarantines, restrictions on travel and mandatory closures of businesses. Certain states and cities, including where we or the third parties with whom we engage operate, have also reacted by instituting quarantines, restrictions on travel, “shelter in place” rules, restrictions on types of business that may continue to operate and/or restrictions on the types of construction projects that may continue.

The extent to which the COVID-19 pandemic impacts our business, financial condition and results of operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the scope, severity and duration of such pandemic, the actions taken to contain the pandemic or mitigate its impact, as well as the effect of any relaxation of current restrictions within the Cambridge community or regions in which our partners and clinical sites are located, and the direct and indirect economic effects of the pandemic and containment measures, among others. The rapid development and fluidity of this situation precludes any prediction as to the full adverse impact of the COVID-19 pandemic. Nevertheless, the COVID-19 pandemic may adversely affect our business, financial condition and results of operations, and it has had, and may continue to have, the effect of heightening many of the risks described in this Quarterly Report on Form 10-Q, including but not limited to the below.

- The COVID-19 pandemic has had, and will likely continue to have, an impact on various aspects of our ongoing clinical trials. We remain in active dialog with our contract research organizations, or CROs, and clinical sites to minimize the impact of this pandemic to our gavo-cel and TC-110 Phase 1/2 clinical trials without adversely impacting the safety of patients. Despite our best efforts, it may prove difficult to continue to treat patients in a timely manner and activation of new sites could be delayed, particularly for our clinical trial sites in areas with high rates of community spread. While we anticipate providing additional updates of the Phase 1 portion of the gavo-cel Phase 1/2 clinical trial throughout 2021 and an update from the Phase 1 portion of the TC-110 Phase 1/2 clinical trial in 2021, the effect of the COVID-19 pandemic may impact the exact timing or content of these updates.

- Other potential impacts of the COVID-19 pandemic on our various clinical trials include patient dosing and study monitoring, which may be paused or delayed due to changes in policies at various clinical sites, federal, state, local or foreign laws, rules and regulations, including quarantines or other travel restrictions, prioritization of healthcare resources toward pandemic efforts, including diminished attention of physicians serving as our clinical trial investigators and reduced availability of site staff supporting the conduct of our clinical trials, interruption or delays in the operations of the FDA or other reasons related to the COVID-19 pandemic. If the COVID-19 pandemic continues, other aspects of our clinical trials may be adversely affected, delayed or interrupted, including, for example, site initiation, patient recruitment and enrollment, availability of clinical trial materials and data analysis. Some patients and clinical investigators may not be able to comply with clinical trial protocols and patients may choose to withdraw from our studies or we may have to pause enrollment or we may choose to or be required to pause enrollment and or patient dosing in our ongoing clinical trials in order to preserve health resources and protect trial participants. It is unknown how long these pauses or disruptions could continue.

- We currently rely on third parties, including our CROs, and our contract manufacturing organizations, or CMOs, and other contractors and consultants to, among other things, conduct our preclinical studies and clinical trials, manufacture raw materials, manufacture and supply our product candidates, ship clinical trial samples, perform quality testing and supply other goods and services to run our business. If any such third party is adversely impacted by restrictions resulting from the COVID-19 pandemic, including staffing shortages, production slowdowns and disruptions in delivery systems, our supply chain may be disrupted, which could limit our ability to manufacture our product candidates for our clinical trials and conduct our research and development operations. For example, two vaccines for COVID-19 were granted Emergency Use Authorization by the FDA in late 2020, and more are likely to be authorized in the coming months. 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 for the manufacture of our product candidates, which could lead to delays in these trials.

- Our manufacturing suite at Catapult in Stevenage, UK is now operational, and, subject to the impact of the COVID-19 pandemic, we expect MHRA certification to manufacture in the middle of 2021. However, our ability to manufacture our product candidates at Catapult for our clinical trials will depend on, among other factors, receiving appropriate approvals and clearance from the UK’s Medicines and Healthcare Products Regulatory Agency (MHRA). Limited MHRA resources

and a focus on the COVID-19 pandemic may delay the MHRA's review and approval of our manufacturing suite, and affect our expected manufacturing timelines.

- We have requested that our employees work from home if they are able to perform their duties remotely and limited the number of on-site employees to allow for proper social distancing in our offices and laboratories. Our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. In addition, this could increase our cyber security risk, create data accessibility concerns and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites, research or clinical trial sites and other important agencies and contractors.

- Governmental authorities may modify or expand current "shelter-in-place" advisories or other similar local restrictions and further limit our laboratory operations. Our employees may have limited or no access to our laboratory for an extended period of time and, as a result, this could delay timely completion of preclinical activities, including conducting Investigational New Drug, or IND-, enabling studies or our ability to select future development candidates, and initiation of additional clinical trials for our other product candidates.

- Material shortages may affect our research and development and manufacturing activities and timelines. Increased demand for personal protective equipment, plastics used for pipettes and other laboratory consumables, and other laboratory supplies has led to shortages of some of these materials that we need for our research and development activities, and that our third-party manufacturers need to produce our product candidates. In addition, COVID restrictions on manufacturers and their employees has led to a shortage of personnel to manufacture, package and ship laboratories supplies and consumables, further limiting the available supply. If we, our contract research organizations, our vendors and our third-party manufacturers are not able to obtain materials needed for our laboratory operations, our research and development and the manufacture of our product candidates could be delayed.

- Certain government agencies, such as health regulatory agencies and patent offices, within the U.S. or internationally may experience disruptions in their operations as a result of the COVID-19 pandemic. The Food and Drug Administration, or FDA, and comparable foreign regulatory agencies may have slower response times or be under-resourced to continue to monitor our clinical trials and, as a result, review, inspection and other timelines may be materially delayed. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates.

- The trading prices for our common stock and those of other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the COVID-19 pandemic could materially and adversely affect our business and the value of our common stock.

Risks Related to Our Intellectual Property

Risks Related to Protecting Our Intellectual Property

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

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment and development that are important to our business. If we do not adequately protect 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 file patent applications in the United States and abroad related to our novel product candidates that are important to our business; we may in the future also license or purchase patent applications filed by others. If we are unable to secure or maintain patent protection with respect to our technology and any proprietary products and technology we develop, our business, financial condition, results of operations, and prospects could be materially harmed.

We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect our current and future product candidates or otherwise provide any competitive advantage. In addition, to the extent that we license intellectual property in the future, we cannot assure you that

those licenses will remain in force. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. 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.

Patent positions of life sciences companies can be uncertain and involve complex factual and legal questions. No consistent policy governing the scope of claims allowable in the field of cellular therapy has emerged in the United States. The scope of patent protection in jurisdictions outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in any jurisdiction that we seek patent protection may diminish our ability to protect our inventions, maintain and enforce our intellectual property rights; and, more generally, may affect the value of our intellectual property, including the narrowing of the scope of our patents and any that we may license.

The patent prosecution process is complex, expensive, time-consuming and inconsistent across jurisdictions. We may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent rights at a commercially reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is possible that we will fail to identify important patentable aspects of our research and development efforts in time to obtain appropriate or any patent protection. While we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development efforts, including for example, our employees, corporate collaborators, external academic scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby endangering our ability to seek patent protection. In addition, publications of discoveries in the scientific and scholarly 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. Consequently, we cannot be certain that we were the first to file for patent protection on the inventions claimed in our patents or pending patent applications.

The issuance or grant of a patent is not irrefutable as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. We may in the future, become subject to a third-party pre-issuance submission of prior art or opposition, derivation, revocation, re-examination, post-grant and *inter partes* review, or interference proceeding and other similar proceedings challenging our patent rights or the patent rights of others in the U.S. Patent and Trademark Office (USPTO) or other foreign patent office. An unfavorable determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or extinguish our ability to manufacture or commercialize products without infringing third-party patent rights.

In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Moreover, some of our owned and in-licensed patents and patent applications are, and may in the future be, co-owned with third parties. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

If our efforts to protect the proprietary nature of the intellectual property related to our technologies are not adequate, we may not be able to compete effectively in our market.

Biotechnology and pharmaceutical companies generally, and we in particular, compete in a crowded competitive space characterized by rapidly evolving technologies and aggressive defense of intellectual property. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

We rely upon a combination of patents, confidentiality agreements, trade secret protection and license agreements to protect the intellectual property related to our technologies. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. 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 strengthen our patent position.

It is possible that defects of form in the preparation or filing of our patents or 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 or our partners, collaborators, licensees or licensors fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, licensees or licensors are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patents or patent applications, 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.

Currently, our patents and patent applications are directed to our TRuC-T cells and accompanying technologies. We seek or plan to seek patent protection for our TRuC-T cell platform and product candidates by filing and prosecuting patent applications in the United States and other countries as appropriate. The claims of our patent applications are directed toward various aspects of our product candidates and research programs including compositions of matter, methods of use, and processes. These patent applications, if issued, are expected to expire on various dates from 2036 through 2041, in each case without taking into account any possible patent term adjustments or extensions.

We anticipate additional patent applications will be filed both in the United States and in other countries, as appropriate. However, we cannot predict:

- if and when patents will be issued;
- the degree and range of protection any issued patents will afford us against competitors including whether third parties will find ways to invalidate or otherwise circumvent our patents;
- whether any of our intellectual property will provide any competitive advantage;
- whether any of our patents that may be issued may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications; or
- whether we will need to initiate or defend litigation or administrative proceedings which may be costly regardless of whether we win or lose.

Additionally, we cannot be certain that the claims in our pending patent applications covering composition of matter of our product candidates will be considered patentable by the USPTO, or by patent offices in foreign countries, or that the claims in any of our issued patents will be considered patentable by courts in the United States or foreign countries.

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

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

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

- others may be able to make or use compounds or cells that are similar to the biological compositions of our product candidates but that are not covered by the claims of our patents;
- the active biological ingredients in our current product candidates will eventually become commercially available in biosimilar drug products, and no patent protection may be available with regard to formulation or method of use;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- we have engaged in scientific collaborations in the past and will continue to do so in the future, and such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on our business.

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

In addition to the protection afforded by patents, we seek to rely on trade secret protection, confidentiality agreements, and license agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our product discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. For example, significant elements of our products, including aspects of sample preparation, methods of manufacturing, cell culturing conditions, computational-biological algorithms, and related processes and software, are based on unpatented trade secrets that are not publicly disclosed. Although we require all of our employees to assign their inventions to us, and require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

Courts outside the United States are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. For example, significant elements of our products, including aspects of sample preparation, methods of manufacturing, cell culturing conditions, computational-biological algorithms, and related processes and software, are based on unpatented trade secrets that are not publicly disclosed. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology.

Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties. We have also adopted policies and conduct training that provides guidance on our expectations, and our advice for best practices, in protecting our trade secrets.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our marks of interest and our business may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During the trademark registration process, we may receive Office Actions from the USPTO objecting to the registration of our trademark. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and/or to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Third Party Intellectual Property

We depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others. For example, we have a non-exclusive license for the mesothelin binder incorporated into the TRuC construct for gavo-cel from Harpoon. Harpoon has the ability to terminate our license in the event we materially breach our agreement with Harpoon and fail to cure this breach within sixty days. If the license with Harpoon is terminated, we would need to partner for another mesothelin binder or independently develop our own mesothelin binder. In addition, we cannot prevent Harpoon from also licensing the mesothelin binder we use in gavo-cel to a third-party. If Harpoon licenses the mesothelin binder to another immuno-oncology company, that company could develop a competitive product to gavo-cel.

We are currently, and expect in the future to be, party to material license or collaboration agreements. These agreements typically impose numerous obligations, such as diligence and payment obligations. Any termination of these licenses could result in the loss of significant rights and could harm our ability to commercialize our product candidates. These licenses do and future licenses may include provisions that impose obligations and restrictions on us. This could delay or otherwise negatively impact a transaction that we may wish to enter into.

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

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- 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.

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

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described below. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer.

If we fail to comply with our obligations under our patent licenses with third parties, we could lose license rights that are important to our business.

We are a party to a license agreement with Harpoon, pursuant to which we in-license key patent and patent applications for use in one or more of our product candidates. This existing license imposes various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, Harpoon may have the right to terminate the license, in which event we would not be able to develop or market the products covered by such licensed intellectual property.

We rely on certain of our licensors to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them and may continue to do so in the future. We have limited control over these activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that any licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves.

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

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, reexamination, and post grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

Third parties may assert that we are employing their proprietary technology without authorization. Generally, conducting preclinical and clinical trials and other development activities in the United States is not considered an act of infringement. If gavo-cel, TC-110 or another product candidate is licensed by the FDA, a third party may then seek to enforce its patent by filing a patent infringement lawsuit against us. While we do not believe that any claims that could otherwise have a materially adverse effect on the commercialization of our product candidates, if licensed, are valid and enforceable, we may be incorrect in this belief, or we may not be able to prove it in litigation. In this regard, patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is "clear and convincing," a heightened standard of proof. There may be issued third-party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Patent applications can take many years to issue. There may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, we may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, constructs or molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, could involve

substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, 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, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly.

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

Presently we have rights to certain intellectual property, through licenses from third parties and under patent applications that we own or will own, related to gavo-cel, TC-110 and certain other product candidates. Because additional product candidates may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, while we have patent rights directed to certain TRuC constructs we may not be able to obtain intellectual property to broad TRuC-T cell or engineered TCR-T cell constructs.

Our product candidates may also require specific formulations to work effectively and efficiently and these rights may be held by others. Similarly, efficient production or delivery of our product candidates may also require specific compositions or methods, and the rights to these may be owned by third parties. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. Moreover, the specific antibodies that will be used with our product candidates may be covered by the intellectual property rights of others.

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

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

Risks Related to Intellectual Property Litigation

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

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure.

Post-grant proceedings provoked by third parties or brought by the USPTO may be necessary to determine the validity or priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss

of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Litigation or post-grant proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Risks Related to Intellectual Property Laws

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

Some of our patent applications have been allowed or may be allowed in the future. We cannot be certain that an allowed patent application will become an issued patent. There may be events that cause withdrawal of the allowance of a patent application. For example, after a patent application has been allowed, but prior to being issued, material that could be relevant to patentability may be identified. In such circumstances, the applicant may pull the application from allowance in order for the USPTO to review the application in view of the new material. We cannot be certain that the USPTO will re-allow the application in view of the new material. Further, periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and following the issuance of a patent. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

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

If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post grant review and equivalent proceedings in foreign jurisdictions (such as opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States continues to adapt to wide-ranging patent reform legislation that became effective starting in 2012. Moreover, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, in the case *Assoc. for Molecular*

Pathology v. Myriad Genetics, Inc., the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. While we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, Congress or the USPTO may impact the value of our patents. Similarly, any adverse changes in the patent laws of other jurisdictions could have a material adverse effect on our business and financial condition. Changes in the laws and regulations governing patents in other jurisdictions could similarly have an adverse effect on our ability to obtain and effectively enforce our patent rights.

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

Certain of our key patent families have been filed in the United States, however, we have less robust intellectual property rights outside the United States, and, in particular, we may not be able to pursue generic coverage of the TRuC-T cell platform outside of the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Most of our patent portfolio is at the very early stage. We will need to decide whether and in which jurisdictions to pursue protection for the various inventions in our portfolio prior to applicable deadlines.

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

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

We generally enter into confidentiality and intellectual property assignment agreements with our employees, consultants, and contractors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, those agreements may not be honored and may not effectively assign intellectual property rights to us. Moreover, there may be some circumstances, where we are unable to negotiate for such ownership rights. Disputes regarding ownership or inventorship of intellectual property can also arise in other contexts, such as collaborations and sponsored research. If we are subject to a dispute challenging our rights in or to patents or other intellectual property, such a dispute could be expensive and time consuming. If we were unsuccessful, we could lose valuable rights in intellectual property that we regard as our own.

The intellectual property landscape around adoptive cell therapy is crowded, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. We are aware of certain third-party patents and third-party patent applications in this landscape that may, if issued as patents, be asserted to encompass our technology.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers or our consultants' or contractors' current or former clients or customers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees. If we are not successful, we could lose access or exclusive access to valuable intellectual property.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of our competitors or are in breach of non-competition or non-solicitation agreements with our competitors.

Many of our employees were previously employed at other pharmaceutical companies, including our competitors or potential competitors, in some cases until recently. We may be subject to claims that we or our employees have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of these former employers or competitors. In addition, we have been and may in the future be subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our defense to those claims fails, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Any litigation or the threat thereof may adversely affect our ability to hire employees. A loss of key personnel or their work product could hamper or prevent our ability to commercialize product candidates, which could have an adverse effect on our business, results of operations and financial condition.

If we do not obtain patent term extension and data exclusivity for any of our current or future product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any of our current or future product candidates, one or more 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, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

Risks Related to Government Regulation

Risks Related to Regulatory Approval

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.

We have not previously submitted a Biologics License Application (BLA) to the FDA or similar licensure applications to comparable foreign regulatory authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety, purity and potency for each desired indication. The BLA must also include significant information regarding the manufacturing controls for the product. We expect the novel nature of our product candidates to create further challenges in obtaining regulatory approval. Accordingly, the regulatory approval pathway for our product candidates may be uncertain, complex, expensive and lengthy, and licensure may not be obtained.
We may also experience delays in completing planned clinical trials for a variety of reasons, including delays related to:

- 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 clinical trial sites;
- obtaining approval at each clinical trial site by an IRB or ethics committee;
- recruiting suitable patients to participate in a clinical trial;
- having patients complete a clinical trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- adding new clinical trial sites; or
- manufacturing sufficient quantities of qualified materials under cGMPs, including current Good Tissue Practices (cGTPs), and applying them on a subject by subject basis for use in clinical trials.

We could also experience delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, the IRBs for the institutions in which such trials are being conducted, the Data Monitoring Committee for such trial, or by the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse

side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of our product candidates, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

Securing regulatory approval also requires the submission of information about the biologic manufacturing process and inspection of manufacturing facilities by the relevant regulatory authority. The FDA or comparable foreign regulatory authorities may find deficiencies or fail to approve our manufacturing processes or facilities, whether run by us or our commercial manufacturing organizations (CMOs). In addition, if we make manufacturing changes to our product candidates in the future, we may need to conduct additional preclinical studies to bridge our modified product candidates to earlier versions.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may ultimately lead to the denial of regulatory approval of our product candidates.

Even if 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 and efficacy of the product candidate. The FDA may also require a risk evaluation and mitigation strategy, or REMS, program in order to license our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, 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, cGTPs and good clinical practices (GCPs) for any clinical trials that we conduct post-licensure. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, 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;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS, which may include distribution or use restrictions;
- requirements to conduct additional post-market clinical trials to assess the safety of the product;
- 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 and other regulatory authorities' 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 action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

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

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

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

- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory authority that any of our product candidates are safe, potent and pure;
- the FDA's or the applicable foreign regulatory agency's disagreement with our trial protocol or the interpretation of data from preclinical studies or clinical trials;
- our inability to demonstrate that the clinical and other benefits of any of our product candidates outweigh any safety or other perceived risks;
- the FDA's or the applicable foreign regulatory agency's requirement for additional preclinical studies or clinical trials;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for licensure;
- the FDA's or the applicable foreign regulatory agency's findings of deficiencies or failure to approve the manufacturing processes or facilities of third-party manufacturers upon which we rely;
- the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of a BLA or other comparable submission in foreign jurisdictions or to obtain licensure of our product candidates in the United States or elsewhere; or
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Any of these factors, many of which are beyond our control, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects. Of the large number of biological products in development, only a small percentage successfully complete the FDA or other regulatory approval processes and are commercialized. Even if we eventually complete clinical testing and receive licensure from the FDA or applicable foreign regulatory authorities for any of our product candidates, the FDA or the applicable foreign regulatory agency may grant licensure contingent on the performance of costly additional clinical trials which may be required after licensure. The FDA or the applicable foreign regulatory agency also may license our product candidates for a more limited indication or a narrower patient population than we originally requested, and the FDA, or applicable foreign regulatory agency, may not license our product candidates with the labeling that we believe is necessary or desirable for the successful commercialization of such product candidates.

In addition, even if the trials are successfully completed, preclinical and clinical data are often susceptible to varying interpretations and analyses, and we cannot guarantee that the FDA or comparable foreign regulatory authorities will interpret the results as we do, and more clinical trials could be required before we submit our product candidates for approval. To the extent that the results of the clinical trials are not satisfactory to the FDA or comparable foreign regulatory authorities for support of 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 clinical trials in support of potential approval of our product candidates.

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

A variety of risks associated with marketing our product candidates, if approved, internationally could materially adversely affect our business.

We plan to seek regulatory approval of our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with international operations may materially adversely affect our ability to attain or maintain profitable operations.

We may seek orphan drug status for gavo-cel, TC-110 and some of our other future product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced.

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 greater than 200,000 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. Orphan drug designation must be requested 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 for a particular active ingredient 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 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 drugs that have a different active ingredient for use in treating the same indication or disease. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

We received orphan drug designation for the treatment of mesothelioma with gavo-cel and we have applied for orphan drug designation for the treatment of cholangiocarcinoma with gavo-cel. We received orphan drug designation for the treatment of acute lymphoblastic leukemia with TC-110 and we may seek orphan drug designation for TC-110 and some or all of our other future product candidates in additional orphan indications in which there is a medically plausible basis for the use of these products. Even when we obtain orphan drug designation, exclusive marketing rights in the United States may be limited if we seek licensure 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 the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, although we intend to seek orphan drug designation for other product candidates, we may never receive such designations.

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

We plan to seek a Breakthrough Therapy designation for gavo-cel and TC-110 and may seek Breakthrough Therapy designation for some or all of our future product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug, or biologic, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Biologics designated as breakthrough therapies by the FDA may also be eligible for other expedited approval programs, including Accelerated Approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or licensure compared to candidate products considered for licensure under non-expedited FDA review procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product no longer meets the conditions for qualification. Thus,

even though we intend to seek Breakthrough Therapy designation for gavo-cel or TC-110 and some or all of our future product candidates for the treatment of various cancers, there can be no assurance that we will receive breakthrough therapy designation.

A Fast Track designation by the FDA, even if granted for gavo-cel, TC-110 or any other future product candidate(s), may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

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 to FDA for FDA Fast Track designation for a particular indication. We plan to seek Fast Track designation for gavo-cel and TC-110 and may seek Fast Track designation for certain of our future product candidates, but there is no assurance that the FDA will grant this status to any of our proposed 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 if we do receive Fast Track designation, we may not experience a faster development process, review or licensure 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.

Accelerated approval by the FDA, even if granted for gavo-cel and TC-110 or any other future product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.

We plan to seek approval of gavo-cel and TC-110, and may seek approval of future product candidates using FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate 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 (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 biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence. 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. Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance of ultimate FDA approval.

Regulatory requirements in the United States and abroad governing cell therapy products have changed frequently and may continue to change in the future, which could negatively impact our ability to complete clinical trials and commercialize our product candidates in a timely manner, if at all.

Regulatory requirements in the United States and abroad governing cell therapy products have changed frequently and may continue to change in the future. The FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research to consolidate the review of gene therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee, among others, to advise this review. Recently, the National Institutes of Health proposed to revise its guidelines for overseeing gene therapy research, including deleting the protocol registration and reporting requirements for certain therapies and eliminating Recombinant DNA Advisory Committee review and reporting requirements for human gene transfer research.

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.

In both domestic and foreign markets, successful sales of our product candidates, if licensed, will depend on the availability of adequate coverage and reimbursement from third-party payors. In addition, because our product candidates represent new approaches to the treatment of cancer, we cannot accurately estimate the potential revenue from our product candidates.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance.

Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. 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 approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. 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.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

We intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we obtain licensure in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the European Union (EU), the pricing of biologics is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future healthcare reform measures.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. In particular, in 2010, Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA) was enacted. The Affordable Care Act and its implementing regulations, among other things, revised the methodology by which rebates owed by manufacturers to the state and federal government for covered outpatient drugs and certain biologics, including our product candidates, under the Medicaid Drug Rebate Program are calculated, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs and provided incentives to programs that increase the federal government's comparative effectiveness research.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the United States Supreme Court; the former Trump Administration issued various Executive Orders which eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices; and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. The United States Supreme Court is expected to rule on a legal challenge to the constitutionality of the ACA in early 2021. The implementation of the ACA is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Litigation and legislation related to the ACA are likely to continue, with unpredictable and uncertain results. We cannot predict what affect further changes to the ACA would have on 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 and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, as well as subsequent legislation, these reductions have been suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. Proposed legislation, if passed, would extend

this suspension until the end of the pandemic. In January 2013, then President Obama signed into law the American Taxpayer Relief Act of 2012 (ATRA), which delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. ATRA also, among other things, 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.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. The former Trump administration's budget proposal for fiscal year 2021 included a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the former Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. In addition, the Trump administration previously issued a plan to lower drug prices and reduce out of pocket costs of drugs. Under this blueprint for action, the Trump administration indicated that the U.S. Department of Health and Human Services ("HHS") would take steps to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. HHS has already implemented certain of these measures, while others are pending. For example, in May 2019, the Centers for Medicare and Medicaid Services ("CMS") issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020.

It is unclear how these and future developments could affect covered hospitals who might purchase our future products and affect the rates we may charge such facilities for our approved products in the future, if any.

In 2020, former President Trump released several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. In response, the FDA released a final rule 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. 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 will 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. The MFN Model regulations mandate participation by identified Part B providers and would have applied to all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. However, in response to a lawsuit filed by several industry groups, on December 28, the U.S. District Court for the Northern District of California issued a nationwide preliminary injunction enjoining government defendants from implementing the MFN Rule pending completion of notice-and-comment procedures under the Administrative Procedure Act. On January 13, 2021, in a separate lawsuit brought by industry groups in the U.S. District of Maryland, the government defendants entered a joint motion to stay litigation on the condition that the government would not appeal the preliminary injunction granted in the U.S. District Court for the Northern District of California and that performance for any final regulation stemming from the MFN Interim Final Rule shall not commence earlier than 60 days after publication of that regulation in the Federal Register. Further, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada and the MFN Model may materially and adversely affect the price we receive for any of our product candidates. Additionally, on December 2, 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 an order entered by the U.S. District Court for the District of Columbia, the portion of the rule eliminating safe harbor protection for certain rebates related to the sale or purchase of a pharmaceutical product from a manufacturer to a plan sponsor under Medicare Part D has been delayed to January 1, 2023. Further, implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed. Although a number of these, and other proposed measures may require authorization through additional legislation to become effective, it is unclear whether the Biden administration will challenge, reverse, revoke or otherwise modify these recent executive and administrative actions, yet Congress has indicated that it will continue to seek new legislative measures to control drug costs.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care 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 health care programs. These measures could reduce the ultimate demand for our products, once licensed, or put pressure on our product pricing.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

The impact of recent healthcare reform legislation and other changes in the healthcare industry and in healthcare spending on us is currently unknown, and may adversely affect our business model.

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

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. We cannot predict the initiatives that may be adopted in the future, including repeal, replacement or significant revisions to the ACA. 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;
- our ability to obtain coverage and reimbursement approval for a product;
- 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.

Inadequate funding for the FDA, the SEC and other government agencies 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.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, 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 to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA 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. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

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 operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also 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. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

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

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government healthcare programs, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, government authorities and third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

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

Risks Related to Government Regulations Internationally

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

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

reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

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

The withdrawal of the United Kingdom from the European Union, commonly referred to as "Brexit," may disrupt import and export processes between the United Kingdom and the European Union, potentially delaying time-sensitive shipments and adversely affecting our GMP manufacturing operations at Catapult, and may affect the future regulatory regime regarding GMP manufacturing of our product candidates.

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as “Brexit.” Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom formally left the European Union on January 31, 2020. A transition period began on February 1, 2020, during which European Union pharmaceutical law remained applicable to the United Kingdom, which ended on December 31, 2020. During this 11-month period, the UK continued to follow all of the EU’s rules and its trading relationship remained the same. The United Kingdom and the European Union have signed a EU-UK Trade and Cooperation Agreement (the TCA), which became provisionally applicable on January 1, 2021 and will become formally applicable once ratified by both the United Kingdom and the European Union. This agreement provides details on how some aspects of the United Kingdom and European Union’s relationship will operate going forwards however there are still many uncertainties. This lack of clarity on future United Kingdom laws and regulations and their interaction with European Union laws and regulations could add legal risk, uncertainty, complexity and cost to our operations.

We have contracted with the Cell Therapy Catapult Limited (Catapult) to occupy a suite with our own personnel in their GMP manufacturing center in Stevenage, United Kingdom. There is a risk that Brexit may disrupt import and export processes due to a lack of administrative processing capacity by the respective United Kingdom and European Union customs agencies that may delay time-sensitive shipments of equipment and materials from the European Union that are required for GMP manufacturing in our Catapult suite. It is also possible that Brexit may negatively affect our ability to attract and retain employees for our operations at Catapult, particularly those from the European Union.

In addition, because the regulatory framework in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU Directives and Regulations, Brexit could materially impact the future regulatory regime which applies to products, and the approval of product candidates, in the United Kingdom, now that the United Kingdom legislation has the potential to diverge from European Union legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the United Kingdom in the long term. The Medicines and Healthcare products Regulatory Agency, or MHRA, the UK medicines and medical devices regulator, has recently published detailed guidance for industry and organizations to follow from January 1, 2021 now the transition period is over, which will be updated as the UK’s regulatory position on medicinal products evolves over time.

Given the lack of comparable precedent, it is unclear what longer term financial, trade and legal implications the withdrawal of the United Kingdom from the European Union will have and how such withdrawal would affect us. The long-term impact of Brexit, including on our business and our industry, will depend on how the terms of the TCA take effect in practice and any further terms that are negotiated in relation to the United Kingdom’s future relationship with the European Union. We are continuing to closely monitor the Brexit developments in order to determine, quantify and proactively address changes as they become clear.

Risks Related to Employee Matters and Managing Growth

Risks Related to Employee Matters

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 Chief Financial Officer, our Chief Scientific Officer, our Chief Medical Officer and our Chief People Officer. The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and an inability to find suitable replacements could result in delays in product development and harm our business.

We conduct our operations at our facility in Cambridge, Massachusetts. This region is headquarters to many other biopharmaceutical companies and many academic and research institutions. 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. Changes to U.S. immigration and work authorization laws and regulations, including those that restrain the flow of scientific and professional talent, can be significantly affected by political forces and levels of economic activity. Our business may be materially adversely affected if legislative or administrative changes to immigration or visa laws and regulations impair our hiring processes and goals or projects involving personnel who are not U.S. citizens.

To encourage 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. 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.

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 regulations of the FDA and other similar foreign regulatory authorities, provide true, complete and accurate information to the FDA and other similar foreign regulatory authorities, 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 and regulations will increase significantly, and our costs associated with compliance with such laws and regulations 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. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act or federal civil money penalties statute. On December 2, 2020, the Office of Inspector General, or OIG, published further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. This rule (with exceptions) became effective January 19, 2021. Implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed. We continue to evaluate what effect, if any, the rule will have on our business;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other third-party payors that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (for example, public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;
- the federal Physician Payments Sunshine Act, created under the ACA and its implementing regulations, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to HHS information related to payments or other transfers of value made to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made during the previous year to certain non-physician providers such as physician assistants and nurse practitioners; and
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payor.

We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter employee misconduct, 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 with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. 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 criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, and exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, reputational harm, and we may be required to curtail or restructure our operations, any of which could adversely affect our ability to operate our business and our results of operations.

The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU Member States, such as the U.K. Bribery Act 2010, or the Bribery Act. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation (GDPR), which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR 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 our European activities.

Risks Related to Growing Our Organization

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

As of March 1, 2021, we had 118 full-time employees. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, sales, marketing, financial and other personnel, as well as additional facilities to expand our operations. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining 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 any future 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 substantially all aspects of regulatory approval, clinical trial management and manufacturing. 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.

Further, we anticipate growth in our business operations, which would necessitate the addition of new laboratory and/or office space. This future growth could create strain on our organizational, administrative, and operational infrastructure, including laboratory operations and quality control. There is no guarantee that we will be able to manage the expansion of our facilities and operations, or that our systems, procedures or controls will be adequate to support our expanded facilities and operations. There is also no guarantee that we will be able to build out, acquire, or enter into agreements to lease facilities to support our growth.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, or we are not able to effectively build out new facilities to accommodate this expansion, 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.

We currently have no marketing and sales organization and have no experience in marketing products. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if licensed, we may not be able to generate product revenue.

We currently have no sales, marketing or distribution capabilities and have no experience in marketing products. We intend to develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel.

If we are unable or decide not to establish internal sales, marketing and distribution capabilities, we will pursue collaborative arrangements regarding the sales and marketing of our products, if licensed. However, there can be no assurance that we will be able to establish or maintain such collaborative arrangements, or if we are able to do so, that they will have effective sales forces. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates.

There can be no assurance that we will be able to develop in-house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product in the United States or overseas.

Risks Related to our Common Stock

Risks Related to Volatility in the Trading of Our Common Stock

Our stock price has been and will likely continue to be volatile. Securities class action or other litigation involving our company or members of our management team could also substantially harm our business, financial condition and results of operations.

The trading price of our common stock is likely to be highly volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price of our common stock may be influenced by many factors, including:

- the timing and results of clinical trials of gavo-cel, TC-110 and any other product candidates and our ongoing, planned or any future preclinical studies, clinical trials or clinical development programs;
- the commencement, enrollment, or results of clinical trials of our product candidates or any future clinical trials we may conduct, or changes in the development status of our product candidates;
- adverse results or delays in preclinical studies and clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial, or to terminate an existing clinical trial;
- any delay in our regulatory filings or any adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- changes in laws or regulations applicable to our products, including but not limited to clinical trial requirements for approvals;
- adverse developments concerning our manufacturers or our manufacturing plans;
- 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;
- our failure to commercialize our product candidates;
- 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 cancer target markets;
- our ability to successfully treat additional types of cancers or at different stages;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or immunotherapy in particular, 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; 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 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. If the market price of our common stock does not exceed your purchase price, you may not realize any return on your investment in us and may lose some or all of your investment. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would harm our business, operating results, or financial condition.

An active, liquid and orderly trading market for our common stock may not be sustained.

In February 2019, we closed our IPO and our common stock began trading on The Nasdaq Global Select Market. Prior to our IPO, there was no public trading market for shares of our common stock. Although we completed our IPO and our common stock is listed and trading on The Nasdaq Global Select Market, an active trading market for our shares may not be sustained. If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at or above the prices at which they acquired their shares or sell their shares at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration.

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.

In connection with our IPO, our officers, directors and substantially all of our stockholders agreed to be subject to a contractual lock-up with our underwriters. These lock-up agreements expired on August 13, 2019. If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market the trading price of our common stock could decline. As of December 31, 2020, we have a total of 33,516,795 shares of common stock outstanding. In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our 2018 Plan and our 2018 Employee Stock Purchase Plan adopted in connection with the IPO will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, Rule 144 and Rule 701 under the Securities Act of 1933, as amended (the Securities Act). If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The holders of 17,276,913 shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. 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.

Risks Related to Our Status as an “Emerging Growth Company” and a Smaller Reporting Company

We are an emerging growth company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth 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 (JOBS Act) enacted in April 2012. 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 (Sarbanes-Oxley Act), reduced disclosure obligations regarding executive compensation in our Annual Report, our other 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 our IPO, 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 closing of our IPO, (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 avail ourselves of this exemption from complying with new or revised accounting standards and, therefore, will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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 Annual Report, our other 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.

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

We are considered a "smaller reporting company" under Rule 12b-2 of the Exchange Act. We are therefore entitled to rely on certain reduced disclosure requirements, such as an exemption from providing selected financial data and executive compensation information. These exemptions and reduced disclosures in our SEC filings due to our status as a smaller reporting company also mean our auditors are not required to review our internal control over financial reporting and may make it harder for investors to analyze our results of operations and financial prospects. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our common stock prices may be more volatile. We will remain a smaller reporting company until our public float exceeds $250 million or our annual revenues exceed $100 million and we have a public float greater than $700 million.

Risks Related to Insider Control

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

As of March 1, 2021, our executive officers, directors, and 5% stockholders beneficially owned approximately 50% of our voting stock. Therefore, these stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control 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.

Risks Related to Operating as a Public Company

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

As a public company, we have incurred and will continue to incur significant legal, accounting, and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, which require, among other things, that we file with the Securities and Exchange Commission (SEC), annual, quarterly, and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and The Nasdaq Global Select Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (the Dodd-Frank Act) was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas, such as "say on pay" and proxy access. Recent legislation permits emerging growth companies to implement many of these requirements over a longer period and up to five years from the pricing of our IPO. We are taking advantage of this legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment, and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

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

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 chairperson 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 not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds 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 acquirers 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 bylaws designate certain courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Our amended bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the 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 fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws (including the interpretation, validity or enforceability thereof) or (iv) any action asserting a claim that is 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 or the Exchange Act. In addition, our amended and restated bylaws will further provide that unless we consent in writing to the selection of an alternate forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the "Federal Forum Provision"). 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 Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with U.S. federal securities laws and the rules and regulations thereunder.

We recognize that the Delaware Forum Provision and the Federal Forum Provision in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims. 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. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the United States 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.

Risks Related to Tax and Accounting

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

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change taxable income may be limited. As a result of our most recent private placements and other transactions that have occurred over the past three years, we may have experienced, and, may experience, an "ownership change." We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As of December 31, 2020, we have cumulative net operating loss carryforwards of approximately $126.4 million and $129.0 million available to reduce federal and state taxable income, respectively, of which $122.3 million of federal net operating losses will carryforward indefinitely, with the remaining federal and state losses beginning to expire in 2035. In addition, we have cumulative federal and state tax credit carryforwards of $5.6 million and $2.4 million, respectively, available to reduce federal and state income taxes which will begin to expire in 2035 and 2031, respectively. Our net operating loss carryforwards and tax credit carryforwards may be limited as a result of certain ownership changes, as defined under Sections 382 and 383 of the Code. This limits the annual amount of these tax attributes that can be utilized to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on our value immediately prior to an ownership change. Subsequent ownership changes may affect the limitation in future years. Under the Tax Cuts and Jobs Act, federal net operating losses generated after December 31, 2017 will not be subject to expiration.

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.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an "emerging growth company" under the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act. We could be an "emerging growth company" for up to five years. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation.

General Risk Factors

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. In addition, we may enter into agreements that prohibit us from paying cash dividends without prior written consent from our contracting parties, or which other terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock, which may never occur.

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

As widely reported, global credit and financial markets have experienced extreme volatility and disruptions in the past several years, 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. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions.

If the current equity and credit markets deteriorate, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

In February 2019, we raised aggregate net cash proceeds of approximately $77.1 million in our IPO. On July 31, 2020, we completed the sale of 9.2 million shares of stock in at a public offering price of $15.50 per share. We raised net cash proceeds of approximately $133.6 million from the offering. As of December 31, 2020, we had cash, cash equivalents and short-term investments of $228.0 million. While we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents and short-term investments since December 31, 2020, no assurance can be given that deterioration of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or our ability to meet our financing objectives. Furthermore, our stock price may decline due in part to the volatility of the stock market and the general economic downturn.

Changes in tax law 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. For example, the Tax Cuts and Jobs Act (the TCJA), was enacted in 2017 and significantly reformed the Internal Revenue Code of 1986, as amended. The TCJA, among other things, included significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, a limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), a limitation of the deduction for net operating losses to 80% of current year taxable income and the elimination of net operating loss carrybacks (though any such net operating losses may be carried forward indefinitely), and the modification or repeal of many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as “orphan drugs”). Additionally, on March 27, 2020, President Trump signed into law the Coronavirus Aid, Relief, and Economic Security Act (the CARES Act), which, among other things, suspends the 80% limitation on the deduction for net operating losses in taxable years beginning before January 1, 2021, permits a 5-year carryback of net operating losses arising in taxable years beginning after December 31, 2017 and before January 1, 2021, and generally caps the limitation on the deduction for net interest expense at 50% of adjusted earnings for taxable years beginning in 2019 and 2020. It cannot be predicted whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or issued, which could result in an increase in our or our stockholders’ tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law.

Our internal computer systems, or those used by our third-party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of the development programs of our product candidates.

Despite the implementation of security measures, our internal computer systems and those of our current and future CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, and telecommunication and electrical failures. While we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of data from completed or future preclinical studies and clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. 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.

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

Our operations, and those of our CROs, CMOs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical pandemics or 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 rely on third-party manufacturers to produce and process our product candidates on a

patient-by-patient basis. 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.

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 planned clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if 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:

- decreased demand for our product candidates or products that we may develop;
- 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.

Failure to obtain or retain 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. Although we have clinical trial insurance, our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient 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.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company, the trading price for our stock would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who cover 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

Not Applicable.

Item 2. Properties.

List of material office locations as of December 31, 2020.

Location	Use of Space	Square Feet	Expiration
Cambridge, Massachusetts	Office and lab	23,000	June 2025
Cambridge, Massachusetts	Office	5,000	December 2021
Cambridge, Massachusetts	Office and lab	14,000	December 2023
Waltham, Massachusetts	Lab	600	April 2022
Stevenage, United Kingdom	Office and lab	5,000	February 2022

We believe that our office and laboratory space is sufficient to meet our needs for the foreseeable future.

Item 3. Legal Proceedings

From time to time, we may be subject to legal proceedings and claims in the ordinary course of business. We are not currently aware of any such proceedings or claims that we believe will have, individually or in the aggregate, a material adverse effect on our business, financial condition or results of operations.

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.

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades under the symbol "TCRR" on the Nasdaq Global Select Market and has been publicly traded since February 14, 2019. Prior to this time, there was no public market for our common stock.

Holders of Our Common Stock

As of March 1, 2021, there were approximately 16 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain any future earnings to fund the development and expansion of our business, and therefore we do not anticipate paying cash dividends on our common stock in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will depend on our results of operations, financial condition, capital requirements, contractual restrictions and other factors deemed relevant by our board of directors.

Securities Authorized for Issuance Under Equity Compensation Plans

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.

Recent sales of unregistered securities

Use of Proceeds from Initial Public Offering

In February 2019, we completed the initial public offering of our common stock (the IPO) pursuant to which we issued and sold 5,750,000 shares of our common stock at a price to the public of $15.00 per share.

All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333- 229066), which was declared effective by the SEC on February 13, 2019. Following the sale of all shares, including shares sold pursuant to the underwriters' option to purchase an additional 750,000 shares exercised in February 2019, in connection with the closing of our IPO, the offering terminated. Jefferies, SVB Leerink and BMO Capital Markets acted as joint book-running managers and Wedbush PacGrow and China Renaissance acted as lead manager of our initial public offering.

We received aggregate gross proceeds from our IPO of approximately $86.3 million, or aggregate net cash proceeds of approximately $77.1 million after deducting underwriting discounts and commissions and offering expenses. None of the underwriting discounts and commissions or offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any of our affiliates. Information related to use of proceeds from registered securities is incorporated herein by reference to the "Use of Proceeds" section of our final prospectus related to the IPO.

As of December 31, 2020, we have used all of the net proceeds, primarily to advance the research and development of our product candidates for our initial indications, to progress additional pipeline development candidates and invest in our platform and for working capital and general corporate purposes.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data

You should read the following selected financial data together with our consolidated financial statements and the related notes appearing at the end of this Annual Report on Form 10-K and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section.

We have derived the Consolidated Statements of Operations for the years ended December 31, 2020 and 2019 and the Consolidated Balance Sheet as of December 31, 2020 and 2019 from audited consolidated financial statements appearing elsewhere in this Annual Report. The Consolidated Statement of Operations for the year ended December 31, 2018 and Balance Sheet as of December 31, 2018 are derived from our audited consolidated financial statements that are not included in this Form 10-K. Our historical results are not necessarily indicative of the results that may be expected in any future period.

	For the Years Ended December 31,		
	2020	2019	2018
	(in thousands)		
Consolidated Statements of Operations			
Research and development	$ 51,980	$ 37,488	$ 19,673
General and administrative	16,720	13,894	6,780
Total operating expenses	68,700	51,382	26,453
Loss from operations	(68,700)	(51,382)	(26,453)
Interest income, net	1,737	3,885	2,202
Loss before income tax expense	$ (66,963)	$ (47,497)	$ (24,251)

	Years Ended December 31,		
	2020	2019	2018
	(in thousands)		
Consolidated Balance Sheet data			
Cash, cash equivalents, and investments	$ 227,986	$ 158,124	$ 123,167
Working capital[1]	226,698	155,652	120,028
Total assets	246,195	168,528	129,433
Redeemable convertible preferred stock	—	—	209,230
Accumulated deficit	(249,715)	(182,591)	(85,590)
Total stockholders' equity (deficit)	236,548	160,449	(85,696)

[1] Working capital is calculated as current assets less current liabilities

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing at the end of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, 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.

Overview

We are a clinical-stage cell therapy company developing a pipeline of novel T cell therapies for patients suffering from cancer by powering the T cell receptor (TCR) with our proprietary, first-in-class TCR Fusion Construct T cells (TRuC-T cells). Designed to overcome the limitations of current cell therapy modalities, our TRuC-T cells specifically recognize and kill cancer cells by harnessing the entire T cell receptor TCR signaling complex, which we believe is essential for T cell therapies to be effective in patients with solid tumors.

Since our inception in May 2015, we have focused significant efforts and financial resources on developing our TRuC platform, establishing and protecting our intellectual property portfolio, conducting research and development of our product candidates, manufacturing drug product material for use in preclinical studies, staffing our company and raising capital. We do not have any products approved for sale and have not generated any revenue from product sales.

Since our inception, we have incurred significant operating losses. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. As of December 31, 2020, we had an accumulated deficit of $249.7 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We expect that our expenses and capital requirements will increase substantially in connection with our ongoing activities, particularly if and as we:

- conduct additional preclinical studies for our product candidates;
- initiate and conduct clinical trials for our product candidates;
- continue to discover and develop additional product candidates;
- acquire or in-license other product candidates and technologies;
- maintain, expand, and protect our intellectual property portfolio;
- hire additional clinical and scientific personnel;
- expand our manufacturing capabilities with third parties and establish manufacturing capabilities in-house;
- seek regulatory approvals for any product candidates that successfully complete clinical trials; and
- add operational, financial, and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, and our operations as a public reporting company.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for our product candidates. If we obtain regulatory approval for any of our product candidates and do not enter into a commercialization partnership, we expect to incur significant expenses related to developing our internal commercialization capability to support product sales, marketing and distribution. Additionally, we expect to incur significant expenses if we acquire and establish our own commercial manufacturing facility, which will be a costly and time-consuming process, and in our operations as a public company.

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

Recent Developments

On January 19, 2021, we entered into an underwriting agreement with Goldman Sachs & Co. LLC, Jefferies LLC, Piper Sandler & Co. and BMO Capital Markets Corp., related to the issuance and sale by us of 4,590,164 shares of the Company's common stock, at a price to the public of $30.50 per share, less underwriting discounts and commissions. The Company granted the Underwriters a 30-day option to purchase, at the public offering price less any underwriting discounts and commissions, up to an additional 688,524 shares of Common Stock. The offering was made pursuant to the Company's shelf registration statement on Form S-3 (File No. 333-236965), filed with the SEC on March 6, 2020 and declared effective on April 28, 2020, as supplemented by a

prospectus supplement dated January 19, 2021 that was filed with the SEC on January 21, 2021. The offering closed on January 22, 2021. The Company received net proceeds from the Offering, after deducting the underwriting discounts and commissions and other estimated offering expenses payable by the Company, of approximately $131.1 million.

Impact of the COVID-19 Pandemic

In December 2019, a novel strain of coronavirus (COVID-19) emerged in Wuhan, Hubei Province, China. COVID-19 has since spread to Europe, the United States and most other countries, and has been declared a pandemic by the World Health Organization. Efforts to contain the spread of COVID-19 have intensified and the United States, including the Commonwealth of Massachusetts where a majority of our operations are located, Europe and Asia, all of which to varying degrees have implemented severe travel restrictions, social distancing requirements, and stay-at-home orders, and such restrictions have had the effect of delaying the commencement of non-COVID-19-related clinical trials, among other restrictions. As a result, the COVID-19 pandemic has caused significant disruptions to the U.S., regional and global economies and has contributed to significant volatility and negative pressure in financial markets. Safety measures in response to the pandemic continue to evolve and vary by jurisdiction.

We have been carefully monitoring the COVID-19 pandemic and its potential impact on our business and have taken important steps to help ensure the safety of employees and their families and to reduce the spread of COVID-19 in our communities while balancing our commitment to conduct our clinical trials. We have requested that our employees work from home if they are able to perform their duties remotely and limited the number of on-site employees to allow for proper social distancing in our offices and laboratories. For those employees on-site, we have implemented stringent safety measures designed to comply with applicable federal, state and local guidelines instituted in response to the COVID-19 pandemic. We have also maintained efficient communication with our partners and clinical sites as the COVID-19 situation has progressed. We have taken these precautionary steps while maintaining business continuity so that we can continue to progress our programs. COVID-19 has significantly impacted the global healthcare system, including the conduct of clinical trials as medical institutions prioritize the treatment of those afflicted with COVID-19. We continue to closely monitor the adverse impact of the COVID-19 pandemic on our operations and ongoing clinical and preclinical development.

The effect of the COVID-19 pandemic on our development timelines for TC-210 and TC-110, and its effect on our ability to manufacture for our clinical trials is uncertain. We believe that we have been able, as of the date of this Annual Report, to mitigate some of the impact from the COVID-19 pandemic on our ongoing clinical programs, however, we have been affected.
The future impact of the COVID-19 pandemic on our industry, the healthcare system, clinical trials and our current and future operations and financial condition will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the scope, severity and duration of the pandemic, the actions taken to contain the pandemic or mitigate its impact, as well as the effect of any relaxation of current restrictions within the Cambridge community or regions in which our partners and clinical sites are located, and the direct and indirect economic effects of the pandemic and containment measures, among others. See “Item 1A. Risk Factors” for a discussion of the potential adverse impact of COVID-19 on our business, results of operations and financial condition.

Components of Our Results of Operations

Operating Expenses

Research and Development Expenses

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

- employee-related expenses, including salaries, benefits and stock-based compensation;
- expenses incurred in connection with the preclinical and clinical development of our product candidates, including under agreements with third parties, such as consultants, contractors and contract research organizations (CROs);
- the cost of acquiring and manufacturing preclinical and clinical trial materials, including under agreements with third parties, such as consultants, contractors and contract manufacturing organizations (CMOs);
- consultant fees and expenses associated with outsourced professional scientific development services;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and insurance; and
- payments made under third-party licensing agreements.

We expense research and development costs as incurred. Any non-refundable advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

We typically use our employee, consultant and infrastructure resources across our development programs. We track certain outsourced development costs by product candidate, but we do not allocate personnel costs or other internal costs to specific product candidates.

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

- the timing and progress of our preclinical studies and clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the progress of the development efforts of parties with whom we may enter into collaboration arrangements;
- our ability to maintain our current research and development programs and to establish new ones;
- our ability to establish licensing or collaboration arrangements;
- our ability to complete investigational new drug application (IND)-enabling studies and successfully submit IND or comparable applications;
- whether we are required by the U.S. Food and Drug Administration (FDA) or similar foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our product candidates or any future product candidates;
- the timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities;
- 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 agencies and develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices (cGMP);
- our ability to demonstrate to the satisfaction of the FDA and similar foreign regulatory authorities 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;
- our ability to establish and enforce intellectual property rights in and to our product candidates or any future product candidates;
- our ability to successfully develop a commercial strategy and thereafter commercialize our product candidates or any future product candidates in the United States and internationally, if licensed for marketing, reimbursement, sale and distribution in such countries and territories, whether alone or in collaboration with others;
- the willingness of physicians, operators of clinics and patients to utilize or adopt any of our product candidates or future product candidates to treat solid and hematologic cancers;
- patient demand for our product candidates and any future product candidates, if licensed;
- competition with other products; and
- continued acceptable safety profile of our therapies following approval.

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

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs, including stock-based compensation, for personnel in executive, finance and administrative functions. General and administrative expenses also include direct and allocated facility-related costs as well as professional fees for legal, patent, consulting, investor and public relations, accounting and audit services. We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance, and director and officer insurance costs as well as investor and public relations expenses associated with operating as a public company.

Other Income, net

Other income, net consists of interest earned on our cash equivalents and investment balances, net of investment charges.

Income Tax Expenses

Income tax expense is generated by investment income of our investment portfolio and the profit margin on our UK operations.

Consolidated Statements of Operations

(in thousands)

	For the Years Ended December 31,		
	2020	**2019**	**Change**
Operating expenses			
Research and development	$ 51,980	$ 37,488	$ 14,492
General and administrative	16,720	13,894	2,826
Total operating expenses	68,700	51,382	17,318
Loss from operations	(68,700)	(51,382)	(17,318)
Interest income, net	1,737	3,885	(2,148)
Loss before income taxes	(66,963)	(47,497)	(19,466)

Comparison of the years ended December 31, 2020 and 2019

Research and development expenses

Research and development expenses were $52.0 million for the year ended December 31, 2020 compared to $37.5 million for the year ended December 31, 2019. The following table summarizes our research and development expenses for the years ended December 31, 2020 and 2019.

(in thousands)

	For the Years Ended December 31,		
	2020	**2019**	**Change**
Clinical program expenses	$ 12,612	$ 9,369	$ 3,243
Platform development expenses	4,601	2,798	1,803
Personnel expenses	23,392	17,911	5,481
Allocated facility expenses	5,763	4,367	1,396
Other expenses	5,612	3,043	2,569
	$ 51,980	$ 37,488	$ 14,492

Spending increased in all areas as we have expanded our research and development efforts. The $14.5 million increase in research and development expense for the year ended December 31, 2020 is primarily attributable to the increase in personnel expenses of $5.5 million due to a significant increase in headcount. Our clinical trial program expenses increased $3.2 million for the year ended December 31, 2020 compared to the year ended December 31, 2019 as our TC-110 clinical trial began during 2020 and our gavo-cell trial has continued. Platform development expenses increased by $1.8 million and other research and development expenses increased by $2.6 million for the year ended December 31, 2020 as compared to the year ended December 31, 2019 as we increased research activities related to our platform, new programs, and enhancements. Allocated facilities costs increased $1.4 million for the year ended December 31, 2020 as compared to the year ended December 31, 2019 as we expanded our lab space.

General and Administrative Expenses

General and administrative expenses were $16.7 million for the year ended December 31, 2020, compared to $13.9 million for the year ended December 31, 2019. The increase in general and administrative expenses was primarily due to an increase in personnel costs of $2.4 million due to our increase in headcount including share-based compensation. Other costs under general and administration expenses increased by $0.4 million as we increased the size and activities of the Company for the year ended December 31, 2020 compared to the year ended December 31, 2019.

Other Income, net

Interest income, net was $1.7 million for the year ended December 31, 2020, compared to $3.9 million for the year ended December 31, 2019. The decrease was due to a significant decrease in interest rates earned on our accounts during 2020 due to the macroeconomic factors impacting the economy.

Liquidity and Capital Resources

Since our inception, we have incurred net losses and generated negative cash flows from operations. Since inception, we have funded our operations with proceeds from the sale of our stock. We have received gross proceeds of $400 million from the sale of our stock since inception, including as a result of proceeds from public offerings. As of December 31, 2020, we had cash, cash equivalents and investments of $228.0 million, and subsequent to December 31, 2020, we raised $131.1 million in net proceeds from our January 2021 stock offering.

Cash flows

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

(in thousands)

	For the Years Ended December 31,	
	2020	2019
Operating activities	$ (56,739)	$ (41,359)
Investing activities	(48,935)	(20,415)
Financing activities	134,699	79,523

Operating Activities

During the year ended December 31, 2020, we used $56.7 million of cash in operating activities, resulting primarily from our net loss of $67.1 million partially offset by non-cash charges of $10.2 million, which related to depreciation and amortization, stock-based compensation. Non-cash charges have increased as we have increased our equipment base and therefore increased depreciation. In addition, as we have increased personnel the number of shares and value of share-based compensation has substantially increased for the year ended December 31, 2020 over the year ended December 31, 2019.

During the year ended December 31, 2019, we used $41.4 million of cash in operating activities, resulting primarily from our net loss of $47.6 million partially offset by non-cash charges of $7.6 million, which related to depreciation and amortization, stock-based compensation, and a net decrease in operating assets and liabilities of $1.4 million. The net decreases in operating assets and liabilities were primarily attributable to the timing in which we paid our vendors.

Investing Activities

During the year ended December 31, 2020, cash used in investing activities was $48.9 million, consisting primarily of purchases of investments net of maturities of $41.8 million and purchases of property and equipment of $7.1 million.

During the year ended December 31, 2019, cash used in investing activities was $20.4 million, consisting primarily of purchases of investments net of maturities of $16.5 million and purchases of property and equipment of $3.9 million.

Financing Activities

During the year ended December 31, 2020, net cash provided by financing activities was $134.7 million from the sale of our stock.

During the year ended December 31, 2019, net cash provided by financing activities was $79.5 million consisting primarily from the sale of stock in our initial public offering.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical studies and clinical trials of our product candidates in development and we will incur additional costs associated with operating as a public reporting company. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to establishing sales, marketing, distribution and other commercial infrastructure to commercialize such products.

In addition, our expenses will increase as we:

- commence enrollment of clinical trials for our product candidates;
- seek regulatory approval for any product candidates that successfully complete preclinical and clinical trials;
- establish manufacturing capabilities in-house for the production of preclinical and clinical supply;
- hire additional clinical, medical, research and operational personnel; and
- maintain, expand, and protect our intellectual property portfolio.

As of December 31, 2020, we had cash, cash equivalents and investments of $228.0 million and subsequent to December 31, 2020, we raised $131.1 million in net proceeds from our January 2021 stock offering. We believe that the net proceeds from sales of our stock, together with our existing cash, cash equivalents and investments, will enable us to fund our operating expenses and capital expenditure requirements at least into 2024. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. 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.

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

Critical Accounting Policies and Significant Judgments and Estimates

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

While our significant accounting policies are described in more detail in Note 3 to our consolidated 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 consolidated financial statements.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the development of our product candidates. We expense research and development costs as incurred.

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

- vendors in connection with preclinical development activities;
- CMOs in connection with the production of preclinical and clinical trial materials; and
- CROs in connection with preclinical studies and clinical trials.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CMOs and CROs that supply, conduct, and manage preclinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of

effort varies from the estimate, we adjust the accrual or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period.

Stock-Based Compensation

We measure stock options and other stock-based awards granted to employees based on their fair value on the date of the grant and recognize compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. We apply the straight-line method of expense recognition to all awards with service-based vesting conditions.
For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed. In the second quarter of 2019, we adopted ASU 2018-07 on a retrospective basis as of January 1, 2019, the beginning of the fiscal year of adoption. Prior to the adoption of ASU 2018-07, share-based payments awards granted to non-employees were measured at fair value on their grant date, subject to periodic remeasurement at each reporting period, and share-based compensation expense was recognized over their vesting terms. After the adoption of ASU 2018-07, the fair value of all outstanding and unvested previously granted non-employee awards was established on January 1, 2019, the effective date of adoption, and share-based compensation expense will continue to be recorded on a straight-line basis over their remaining vesting period, consistent with share-based payment awards granted to employees.

We estimate the fair value of restricted stock at the then-current fair value of our common stock and for other stock-based awards we use the Black-Scholes option-pricing model, which requires subjective assumptions, including the fair value of our common stock, volatility, the expected term of our common stock options, the risk-free interest rate for a period that approximates the expected term of our common stock options, and our expected dividend yield. The assumptions used in our Black-Scholes option-pricing model represent management's best estimates and involve a number of variables, uncertainties and assumptions and the application of management's judgment, as they are inherently subjective. If any assumptions change, our stock-based compensation expense could be materially different in the future.

We do not estimate and apply a forfeiture rate as we have elected to account for forfeitures as they occur.

These assumptions are estimated as follows:

- *Fair Market Value of Common Stock.* Since our IPO, our stock is traded on The Nasdaq Global Select Market. Fair market value of our stock is considered the quoted market price. Prior to our IPO, we have periodically estimated the fair market value of common stock. See "— *Common and Preferred Stock Valuation Methodology*"
- *Volatility.* The expected volatility is based on the historical stock volatility of ours and several comparable publicly traded companies over a sufficient period of time equal to the expected term of the options, as we do not have sufficient trading history to use the volatility of our own common stock.
- *Expected Term.* The expected term represents the period that our stock options are expected to be outstanding. We calculated the expected term using the simplified method based on the average of each option's vesting term and the contractual period during which the option can be exercised, which is typically 10 years following the date of grant.
- *Risk-Free Interest Rate.* The risk-free interest rate was based on the yields of U.S. Treasury securities with maturities commensurate with the expected term of the award.
- *Expected Dividend Yield.* We have not paid dividends on our common stock nor do we expect to pay dividends in the foreseeable future.

Pre-IPO Common and Preferred Stock Valuation Methodology

Prior to our IPO, our common and preferred stock valuations were prepared using a hybrid between the option pricing method (OPM) and the probability-weighted expected return method (PWERM), both of which used market approaches to estimate our enterprise value. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preferences at the time of the liquidity event, such as a strategic sale, a merger or initial public offering. The common stock has a claim on the equity value at an exercise price equal to the remaining value immediately after the preferred stock is liquidated. The OPM is appropriate to use when the range of possible future outcomes is so difficult to predict that forecasts would be highly speculative. The OPM commonly uses the Black-Scholes option pricing model to determine the price of the call option.

In the OPM, the backsolve method can be used to infer the total equity value implied by the pricing and terms of our Series A and Series B preferred stock financing transactions by making assumptions regarding the expected time to liquidity, expected volatility and risk-free interest rate, and then solve for the value of equity such that the implied value for the most recent financing equals the

amount paid. At certain valuation dates, the equity value inferred from the OPM backsolve method was adjusted for company and market specific events that occurred between the financing date and the valuation date.

The PWERM involves a forward-looking analysis of the possible future outcomes, estimation of ranges of future and present value under each outcome and application of a probability factor to each outcome as of the valuation date. Under this method, discrete future outcomes, including an IPO, and non-IPO scenarios, are weighted based on the estimated probability of each scenario.

The hybrid method is generally appropriate to use when the time to a liquidity event is short, making the range of possible future outcomes relatively easy to predict. In the IPO scenario, all shares of preferred stock were assumed to convert to common stock. Accordingly, the estimated equity value was allocated pro rata among our preferred stock and common stock on an as converted basis, which caused the common stock to have a higher relative value per share than under the scenarios captured by the OPM.

The weighting between the PWERM and OPM employed in the hybrid method was based on our board of directors' estimate of the probability of each scenario as of each valuation date. These third-party valuations were performed at various dates, which resulted in valuations of our common stock of $0.74 per share as of September 30, 2016, $1.73 per share as of December 31, 2017, $5.88 per share as of February 28, 2018, $8.05 per share as of August 31, 2018 and $9.23 per share as of December 31, 2018. The fair value of our Series A preferred stock was $1.50 per share as of August 31, 2018 and $1.64 per share as of December 31, 2018. The fair value of our Series B preferred stock was $2.22 per share as of August 31, 2018 and $2.18 per share as of December 31, 2018.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used significantly different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could have been materially different.

Upon the closing of the IPO, all of our outstanding preferred stock converted to common stock and it is no longer necessary for management to estimate the fair value of our common stock in connection with our accounting for granted stock options and other such awards we may grant, as the fair value of our common stock will be determined based on the quoted market price of our common stock.

Royalty Transfer Agreement

In connection with the sale of Series A redeemable convertible preferred stock, certain investors are entitled to receive, in the aggregate, a royalty from us equal to one percent of (i) all global net sales of any of our products and (ii) any license income on intellectual property that was in existence at the time of the Series A preferred stock financing. We have elected to account for this liability at fair value with changes recognized in the Statement of Operations. Given the early stage nature of the underlying technology and inherent risks associated with obtaining regulatory approval and achieving commercialization, we ascribed no value to the royalty agreement at inception and at December 31, 2020 and 2019. We continue to evaluate our scientific progress to assess our obligations under this agreement. There is substantial judgment involved in our assessment.

Recently Issued and Adopted Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 3 to our consolidated financial statements appearing elsewhere in this Annual Report.

Emerging Growth Company Status

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 (JOBS Act), and are eligible to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth 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 avail ourselves of this exemption from complying with new or revised accounting standards and, therefore, will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an emerging growth company, we may rely on certain of these exemptions, 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.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Information required by this Item is not applicable as we are electing scaled disclosure requirements available to Smaller Reporting Companies with respect to this Item.

Item 8. Financial Statements

TCR2 THERAPEUTICS INC.

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
TCR2 Therapeutics Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of TCR2 Therapeutics Inc. and subsidiaries (the Company) as of December 31, 2020 and 2019, the related consolidated statements of operations, comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, 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 consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits 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 consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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

/s/ KPMG LLP

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

Boston, Massachusetts
March 16, 2021

TCR2 THERAPEUTICS INC.

CONSOLIDATED BALANCE SHEETS
(amounts in thousands, except share data)

	December 31, 2020	December 31, 2019
Assets		
Current assets		
Cash and cash equivalents	$ 94,155	$ 65,296
Investments	133,831	92,828
Prepaid expenses and other current assets	7,552	5,061
Total current assets	235,538	163,185
Property and equipment, net	10,013	4,926
Restricted cash	583	417
Deferred offering costs	61	-
Total assets	$ 246,195	$ 168,528
Liabilities and stockholders' equity		
Accounts payable	$ 2,448	$ 2,483
Accrued expenses and other current liabilities	6,392	5,050
Total current liabilities	8,840	7,533
Other liabilities	807	546
Total liabilities	9,647	8,079
Commitments and contingencies (Note 7)		
Stockholders' equity		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized, no shares issued or outstanding at December 31, 2020 and December 31, 2019, respectively.	-	-
Common stock, $0.0001 par value; 150,000,000 shares authorized; 33,516,795 and 24,050,936 shares issued; 33,516,795 and 23,981,109 shares outstanding at December 31, 2020 and 2019, respectively.	3	2
Additional paid-in capital	486,197	342,896
Accumulated other comprehensive income	63	142
Accumulated deficit	(249,715)	(182,591)
Total stockholders' equity	236,548	160,449
Total liabilities and stockholders' equity	$ 246,195	$ 168,528

See notes to consolidated financial statements

TCR2 THERAPEUTICS INC.

CONSOLIDATED STATEMENTS OF OPERATIONS
(amounts in thousands, except share and per share data)

	Years Ended December 31,	
	2020	**2019**
Operating expenses		
Research and development	$ 51,980	$ 37,488
General and administrative	16,720	13,894
Total operating expenses	68,700	51,382
Loss from operations	(68,700)	(51,382)
Interest income, net	1,737	3,885
Loss before income tax expense	(66,963)	(47,497)
Income tax expense	161	102
Net loss	(67,124)	(47,599)
Accretion of redeemable convertible preferred stock to redemption value	-	(49,900)
Net loss attributable to common stockholders	$ (67,124)	$ (97,499)
Per share information		
Net loss per share of common stock, basic and diluted	$ (2.40)	$ (4.62)
Weighted average shares outstanding, basic and diluted	27,990,564	21,104,195

See notes to consolidated financial statements

TCR2 THERAPEUTICS INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(amounts in thousands)

	Years Ended December 31,	
	2020	**2019**
Net loss	$ (67,124)	$ (47,599)
Unrealized gain (loss) on investments, net	(79)	248
Comprehensive loss	$ (67,203)	$ (47,351)

See notes to consolidated financial statements

TCR2 THERAPEUTICS INC.

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

(amounts in thousands, except share data)

	Redeemable Convertible Preferred Stock									
	Series A		Series B		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2018	44,500,001	$ 72,980	62,500,000	$ 136,250	726,990	$ -	$ -	$ (85,590)	$ (106)	$ (85,696)
Reclassification of shares issued and previously subject to repurchase	-	-	-	-	117,785	-	52	-	-	52
Exercise of stock options	-	-	-	-	111,035	-	391	-	-	391
Stock-based compensation expense	-	-	-	-	-	-	6,702	-	-	6,702
Accretion of redeemable preferred stock to redemption value	-	34,789	-	15,111	-	-	(498)	(49,402)	-	(49,900)
Conversion of shares upon IPO	(44,500,001)	(107,769)	(62,500,000)	(151,361)	17,275,299	2	259,128	-	-	259,130
Initial public offering, net of issuance costs	-	-	-	-	5,750,000	-	77,121	-	-	77,121
Unrealized gain on investments	-	-	-	-	-	-	-	-	248	248
Net loss	-	-	-	-	-	-	-	(47,599)	-	(47,599)
Balance at December 31, 2019	-	$ -	-	$ -	23,981,109	$ 2	$ 342,896	$ (182,591)	$ 142	$ 160,449
Issuance of common stock, net of issuance costs	-	-	-	-	9,200,000	1	133,570	-	-	133,571
Reclassification of shares issued and previously subject to repurchase	-	-	-	-	69,826	-	51	-	-	51
Exercise of stock options	-	-	-	-	265,860	-	1,188	-	-	1,188
Stock-based compensation expense	-	-	-	-	-	-	8,492	-	-	8,492
Unrealized loss on investments	-	-	-	-	-	-	-	-	(79)	(79)
Net loss	-	-	-	-	-	-		(67,124)	-	(67,124)
Balance at December 31, 2020	-	$ -	-	$ -	33,516,795	$ 3	$ 486,197	$ (249,715)	$ 63	$ 236,548

See notes to consolidated financial statements

TCR2 THERAPEUTICS INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(amounts in thousands)

	Twelve Months Ended December 31,	
	2020	**2019**
Operating activities		
Net loss	$ (67,124)	$ (47,599)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation and amortization	1,592	862
Stock-based compensation expense	8,492	6,702
Accretion on investments	(702)	(225)
Deferred tax liabilities	131	-
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,101)	(3,057)
Accounts payable	451	(179)
Accrued expenses and other liabilities	1,522	2,137
Cash used in operating activities	(56,739)	(41,359)
Investing activities		
Purchases of equipment	(7,164)	(3,879)
Purchases of investments	(152,812)	(126,261)
Proceeds from sale or maturity of investments	111,041	109,725
Cash used in investing activities	(48,935)	(20,415)
Financing activities		
Proceeds from public offering of common stock, net of issuance costs	133,571	79,132
Proceeds from the exercise of stock options	1,189	391
Deferred offering costs	(61)	-
Cash provided by financing activities	134,699	79,523
Net change in cash, cash equivalents, and restricted cash	29,025	17,749
Cash, cash equivalents, and restricted cash at beginning of year	65,713	47,964
Cash, cash equivalents, and restricted cash at end of period	$ 94,738	$ 65,713
Supplemental disclosure of noncash activities		
Conversion of redeemable convertible preferred stock to common stock	$ -	$ 259,130
Accretion of redeemable convertible preferred stock to redemption value	$ -	$ 49,900
Property and equipment additions in accounts payable	$ 611	$ 270

See notes to consolidated financial statements

1. Organization and Description of Business

TCR2 Therapeutics Inc. (the Company) is a clinical-stage immunotherapy company developing the next generation of novel T cell therapies for patients suffering from cancer. The Company was incorporated under the laws of the State of Delaware on May 29, 2015 under the name TCR2, Inc. In November 2016, the Company changed its name to TCR2 Therapeutics Inc. The Company's principal operations are located in Cambridge, Massachusetts.

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated.

Initial Public Offering

In February 2019, the Company completed the initial public offering of its common stock (the IPO) pursuant to which it issued and sold 5,750,000 shares of its common stock at a price to the public of $15.00 per share. The shares began trading on The Nasdaq Global Select Market on February 14, 2019. The aggregate net proceeds received by the Company from the offering were approximately $77,121, after deducting underwriting discounts and commissions and other offering expenses payable by the Company of $9,129. Upon the closing of the IPO, all outstanding shares of redeemable convertible preferred stock converted into 17,275,299 shares of common stock. Additionally, as of the closing of the IPO, the Company is authorized to issue 150,000,000 shares of common stock and 10,000,000 shares of preferred stock.

Reverse Stock Split

On February 1, 2019, the Company effected a 1-for-6.1938 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of the Company's redeemable convertible preferred stock. Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the redeemable convertible preferred stock conversion ratios.

Shelf registration statement

On March 6, 2020, the Company filed a shelf registration statement on Form S-3 (the Shelf), with the Securities and Exchange Commission (SEC), which covers the offering, issuance and sale of up to an aggregate of $300.0 million of the Company's common stock, preferred stock, debt securities, warrants and/or units of any combination thereof. The Company simultaneously entered into a sales agreement with Jefferies LLC, as sales agent, to provide for the issuance and sale by the Company of up to $75.0 million of its common stock from time to time in "at-the-market" offerings under the Shelf, which the Company refers to as the ATM Program. The Shelf was declared effective by the SEC on April 28, 2020. As of December 31, 2020, no sales have been made pursuant to the ATM Program.

Equity offering

On July 31, 2020, the Company closed a public offering of its common stock pursuant to which it issued and sold 9,200,000 shares of its common stock at a price to the public of $15.50 per share. The aggregate net proceeds received by the Company from the offering were approximately $133.6 million after deducting $9.0 million relating to underwriting discounts and commissions and offering expenses.

2. Liquidity

The Company's operations to date have focused on organization and staffing, business planning, raising capital, acquiring technology and assets, manufacturing and conducting clinical and preclinical studies. The Company does not have any product candidates approved for sale and has not generated any revenue from product sales. The Company's product candidates are subject to long development cycles and the Company may be unsuccessful in its efforts to develop, obtain regulatory approval for or market its product candidates.

The Company is subject to a number of risks including, but not limited to, the need to obtain adequate additional funding for the ongoing and planned clinical development of its product candidates. Because of the numerous risks and uncertainties associated with pharmaceutical products and development, the Company is unable to accurately predict the timing or amount of funds required to complete development of its product candidates, and costs could exceed the Company's expectations for a number of reasons,

including reasons beyond the Company's control. The Company is also subject to a number of other risks including possible failure of preclinical studies or clinical trials, the need to obtain marketing approval for its product candidates, the development of new technological innovations by competitors, the need to successfully commercialize and gain market acceptance of any of the Company's products that are approved and uncertainty around intellectual property matters. If the Company does not successfully commercialize any of its products, it will be unable to generate product revenue or achieve profitability.

The Company has incurred net losses from operations since inception. The Company expects to continue to generate losses for the foreseeable future. The Company expects that its cash, cash equivalents and investments as of December 31, 2020 of $228.0 million will be sufficient to fund its operating expenses and capital expenditure requirements through at least twelve months from the date of issuance of these consolidated financial statements.

3. Summary of Significant Accounting Policies

Principles of consolidation and basis of presentation

The accompanying consolidated financial statements have been prepared in conformity with U.S. generally accepted accounting principles (GAAP). Any reference in these notes to applicable guidance is meant to refer to GAAP as found in the Accounting Standards Codification (ASC) and Accounting Standards Updates (ASU) of the Financial Accounting Standards Board (FASB).

Use of estimates

The preparation of the accompanying consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and reported amounts of revenues and expenses during the reporting period. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the fair value of the royalty transfer agreement obligations, the valuation of preferred and common stock prior to the IPO, and the fair value of stock-based compensation awards granted under the Company's equity-based compensation plans. Due to the uncertainty of factors surrounding the estimates or judgments used in the preparation of the consolidated financial statements, actual results may materially vary from these estimates. Estimates and assumptions are periodically reviewed, and the effects of revisions are reflected in the consolidated financial statements in the period they are determined to be necessary.

Concentrations of credit risk and of manufacturing risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents and investments. The Company's cash, cash equivalents and investments are held by financial institutions in the United States. Amounts on deposit may at times exceed federally insured limits. Management believes that the financial institutions are financially sound, and accordingly, minimal credit risk exists with respect to the financial institutions.

As of December 31, 2020, the Company had manufacturing arrangements with vendors for the supply of materials for use in preclinical and clinical studies. If the Company were to experience any disruptions in either party's ability or willingness to continue to provide manufacturing services, the Company may experience significant delays in its product development timelines and may incur substantial costs to secure alternative sources of manufacturing.

Fair value of financial instruments

At December 31, 2020 and 2019, the Company's financial instruments consist of money market funds, commercial paper, agency and corporate bonds, and asset-backed securities are included in investments. The carrying value of investments is the estimated fair value. Fair value is defined as the exchange price that would be received for an asset or 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.

Cash equivalents

The Company considers all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents. As of December 31, 2020 and 2019, cash equivalents consisted of U.S treasuries, corporate bonds and government-backed money market funds.

Investments

As of December 31, 2020, all investments were classified as available-for-sale and were carried at their estimated fair value. Unrealized gains and losses are recorded as a component of accumulated other comprehensive income (loss) until realized. The Company determines the appropriate classification of its investments in debt securities at the time of purchase and re-evaluates such determination at each balance sheet date. The Company periodically reviews its investments in debt securities for impairment and adjusts these investments to their fair value when a decline in market value is deemed to be other than temporary. If losses on these securities are considered to be other than temporary, the loss is recognized in the statement of operations. The Company classifies its available-for-sale marketable securities as current or non-current based on each instrument's underlying effective maturity date and for which the Company has the intent and ability to hold the investment for a period of greater than 12 months. Marketable securities with maturities of less than 12 months are classified as current and are included in investments in the consolidated balance sheets. Marketable securities with maturities greater than 12 months for which the Company has the intent and ability to hold the investment for greater than 12 months are classified as non-current and are included in investments, non-current in the consolidated balance sheets.

Property and equipment

Property and equipment are recorded at cost. Depreciation and amortization are determined using the straight-line method over the estimated useful lives. Expenditures for maintenance and repairs are expensed as incurred while renewals and betterments are capitalized. When property and equipment is sold or otherwise disposed of, the cost and related accumulated depreciation are eliminated from the accounts and any resulting gain or loss is reflected in the consolidated statements of operations.

	Estimated Useful Lives
Laboratory equipment	5 years
Computer hardware and equipment	3 years
Furniture and fixtures	5 - 7 years
Leasehold improvements	Lesser of lease term or estimated useful life.

Impairment of long-lived assets

Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to future undiscounted net cash flows expected to be generated. Impairment charges are recognized at the amount by which the carrying amount of an asset exceeds the fair value of the asset. Assets to be disposed of are reported at the lower of the carrying amount or the fair value less costs to sell. The Company has not recognized any impairment of long-lived assets for the years ended December 31, 2020 and 2019.

Deferred offering costs

The Company capitalizes costs that are directly associated with in-process equity financings until such financings are consummated at which time such costs are recorded against the gross proceeds of the offering. Should the in-process equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statements of operations.

Restricted cash

Cash accounts that are restricted as to withdrawal or usage are presented as restricted cash. Restricted cash includes amounts held as a security deposit in the form of a letter of credit for the Company's leased facilities.

Classification and accretion of redeemable convertible preferred stock

Through the date of the IPO, the Company had classified redeemable convertible preferred stock outstanding and classified outside of stockholders' equity (deficit) because the shares contained certain redemption features that were not solely within the control of the Company. The carrying value of the redeemable convertible preferred stock was accreted to redemption value at the end of each reporting period, up to the date of the IPO, as if the end of the reporting period were the redemption date. Increases to the carrying value of redeemable convertible preferred stock were charged to additional paid-in capital or, in the absence of

additional paid-in capital, charged to accumulated deficit. Upon completion of the IPO during February 2019, all redeemable convertible preferred stock was converted to common stock.

Stock-based compensation

The Company measures employee stock-based awards at grant-date fair value and records compensation expense on a straight-line basis over the requisite service period, which is generally the vesting period of the respective award. Generally, the Company issues awards with only service-based vesting conditions. The Company accounts for forfeitures as they occur.

The Company measures the fair value of stock-based awards granted to non-employees on the date at which the related service is complete. Compensation expense is recognized over the period during which services are rendered by such non-employee consultants until completed. In the second quarter of 2019, the Company adopted ASU 2018-07 on a retrospective basis effective January 1, 2019, the beginning of the fiscal year of adoption. Prior to the adoption of ASU 2018-07, share-based payments awards granted to non-employees were measured at fair value on their grant date, subject to periodic remeasurement at each reporting period, and share-based compensation expense was recognized over their vesting terms. After the adoption of ASU 2018-07, the fair value of all outstanding and unvested previously granted non-employee awards was established on January 1, 2019, the effective date of adoption, and share-based compensation expense will continue to be recorded on a straight-line basis over their remaining vesting period, consistent with share-based payment awards granted to employees.

Common shares issued and stock-options exercised prior to vesting are subject to repurchase by the Company until vested at the lesser of the initial exercise price and the fair market value of the Company's common stock at the time of repurchase. The proceeds from the shares subject to repurchase are classified as a liability and reclassified to equity as the shares vest.

Prior to the IPO, estimating the fair value of stock-based awards required the input of subjective assumptions, including the fair value of the Company's common stock, and, for stock options and warrants, the expected life of the options and stock price volatility. Since the IPO, the Company uses the value of its stock price as quoted on the Nasdaq Global Select Market to determine fair value of the Company's common stock. The Company uses the Black-Scholes option pricing model to value its stock option awards and warrants. The assumptions used in calculating the fair value of stock-based awards represent management's estimates and involve inherent uncertainties and the application of management's judgment. As a result, if factors change and management uses different assumptions, stock-based compensation expense could be materially different for future awards.

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

Research and development expenses

Research and development costs are expensed as incurred and consist primarily of funds for employee wages and funds paid to third parties for the provision of services for product candidate development, clinical and preclinical development and related supply and manufacturing costs, and regulatory compliance costs. At the end of the reporting period, the Company compares payments made to third party service providers to the estimated progress toward completion of the research or development objectives. Such estimates are subject to change as additional information becomes available. Depending on the timing of payments to the service providers and the progress that the Company estimates has been made as a result of the service provided, the Company may record net prepaid or accrued expense relating to these costs.

Upfront milestone payments made to third parties who perform research and development services on the Company's behalf are expensed as services are rendered.

Income taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities 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. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. A reduction in the carrying value of the deferred tax assets is required when it is not more likely than not that such deferred tax assets are not realizable.

(Amounts in thousands, excluding share and per share items or as otherwise noted)

Net loss per share

Basic and diluted net loss per common share is determined by dividing net loss attributable to common stockholders by the weighted-average shares of common stock outstanding during the period. The Company's outstanding redeemable convertible preferred stock contractually entitles the holders of such shares to participate in distributions but contractually does not require the holders of such shares to participate in losses of the Company. Similarly, restricted stock awards granted by the Company entitle the holder of such awards to dividends declared or paid by the Board of Directors, regardless of whether such awards are unvested, as if such shares were outstanding shares of common stock at the time of the dividend. However, the unvested restricted stock awards are not entitled to share in the residual net assets (deficit) of the Company. Accordingly, in periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive shares of common stock are not assumed to have been issued if their effect is anti-dilutive. Therefore, the weighted-average shares used to calculate both basic and diluted loss per share are the same.

The following potentially dilutive securities, on an as converted basis have been excluded from the computation of diluted weighted-average shares outstanding as of December 31, 2020 and 2019, as they would be antidilutive:

	As of December 31,	
	2020	2019
Stock options outstanding	5,011,349	4,189,292
Common stock warrants	203,676	203,676
Employee stock purchase plan	5,141	7,092
Total	5,220,166	4,400,060

Comprehensive loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources (which excludes investments from owners). The Company's only element of other comprehensive loss is unrealized gains and losses on investments.

Reconciliation of cash, cash equivalents and restricted cash as presented in the statements of cash flows

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the consolidated balance sheets to the total of the same such amounts shown in the consolidated statements of cash flows for the years ended December 31, 2020 and 2019.

	As of December 31,	
	2020	2019
Cash and cash equivalents	$ 94,155	$ 65,296
Restricted cash	583	417
Cash, cash equivalents and restricted cash shown in the statements of cash flows	$ 94,738	$ 65,713

Segment information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one consolidated operating segment.

JOBS Act accounting election

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 is (i) 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 consolidated financial statements

(Amounts in thousands, excluding share and per share items or as otherwise noted)

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

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842) which will require lessees to record most operating leases on their balance sheets but recognize the expenses in the statements of operations in a manner similar to current practice. Under the new standard, lessees will be required to recognize a lease liability for the obligation to make lease payments, and an asset for the right to use the underlying asset for the lease term, for all leases with terms longer than 12 months. Leases will be classified as finance or operating, with classification affecting the pattern and classification of expense recognition in the statements of operations. Expenses related to operating leases will be recognized on a straight-line basis, while those determined to be financing leases will be recognized following a front-loaded expense profile, in which interest and amortization are presented separately in the statements of operations. The principal effect on the Company's financial statements will be an increase in assets and liabilities.
The standard will be effective for public business entities for fiscal years beginning after December 15, 2018 and interim periods within those fiscal years. For all other entities and emerging growth companies, the amendments are effective for fiscal years beginning after December 15, 2021. The Company will adopt the new standard beginning January 1, 2022. A modified retrospective transition approach is required, applying the new standard to all leases existing at the date of initial application. The standard includes a number of practical expedients that the Company is evaluating and may elect to apply. The Company expects that the adoption of the new leasing standards will result in the recognition of material right-of-use assets and lease liabilities on the consolidated balance sheets but does not expect it to have a material impact on its results of operations or cash flows.

Recently adopted accounting pronouncements

Beginning January 1, 2019, the Company adopted ASU 2016-18, Statement of Cash Flows (Topic 230) Restricted Cash, which requires entities to show the changes in the total of cash, cash equivalents, restricted cash and restricted cash equivalents in the statement of cash flows. Entities will no longer present transfers between cash and cash equivalents and restricted cash and restricted cash equivalents in the statement of cash flows. The standard requires retrospective application in the consolidated statements of cash flows.

In June 2018, the FASB issued ASU 2018-07, Compensation — Stock Compensation (Topic 718) Improvements to Non-employee Share-Based Payment Accounting. The amendments in this update expand the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from non-employees. Under this ASU, an entity should apply the requirements of Topic 718 to non-employee awards except for specific guidance on inputs to an option pricing model and the attribution of costs (that is, the period of time over which share-based payment awards vest and the pattern of cost recognition over that period). The guidance is applicable to public business entities for fiscal years beginning after December 15, 2018 including interim periods within that fiscal year. For all other entities, the amendments are effective for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020.

In June 2019, the Company adopted ASU 2018-07 on a retrospective basis effective January 1, 2019, the beginning of the fiscal year of adoption. Prior to the adoption of ASU 2018-07, share-based payments awards granted to non-employees were measured at fair value on their grant date, subject to periodic remeasurement at each reporting period, and share-based compensation expense was recognized over their vesting terms. After the adoption of ASU 2018-07, the fair value of all outstanding and unvested previously granted non-employee awards was established on January 1, 2019, the effective date of adoption, and share-based compensation expense will continue to be recorded on a straight-line basis over their remaining vesting period, consistent with share-based payment awards granted to employees. As a result of the adoption of ASU 2018-07, there was no material impact to the financial statements.

4. Investments and Fair Value Measurements

As of December 31, 2020, investments were comprised of the following:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Corporate bonds	$ 34,801	$ 60	$ -	$ 34,861
U.S. Treasury securities	98,967	3	-	98,970
Total	$ 133,768	$ 63	$ -	$ 133,831

(Amounts in thousands, excluding share and per share items or as otherwise noted)

As of December 31, 2019, investments were comprised of the following:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Corporate bonds	$ 92,686	$ 145	$ (3)	$ 92,828

The Company follows FASB's accounting guidance on fair value measurements for financial assets and liabilities measured on a recurring basis. Fair value is defined as the price at which an asset could be exchanged in a current transaction between knowledgeable, willing parties. Where available, fair value is based on observable market prices, or parameters derived from such prices. Where observable prices or inputs are not available, valuation models are applied. This hierarchy requires the use of observable market data when available and to minimize the use of unobservable inputs when determining fair value. These valuation techniques involve some level of management estimation and judgment. The degree of management estimation and judgment is dependent on the price transparency for the instruments, or market, and the instruments' complexity.

The guidance requires fair value measurements to be classified and disclosed in one of the following three categories:

Level 1 — Quoted prices (unadjusted in active markets for identical assets or liabilities)
Level 2 — Inputs other than quoted prices in active markets that are observable either directly or indirectly
Level 3 — Unobservable inputs in which there is little or no market data, which require the Company to develop its own assumptions

The Company has classified assets measured at fair value on a recurring basis as follows as of December 31, 2020:

			Fair Value Measurement Based on		
	Amortized Cost	Fair Value	Quoted Prices in Active Market (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents (1)	$ 89,319	$ 89,319	$ 89,319	$ -	$ -
Corporate bonds	34,801	34,861	-	34,861	-
U.S. Treasury securities	98,967	98,970	-	98,970	-
Total	$ 223,087	$ 223,150	$ 89,319	$ 133,831	$ -

(1) Includes cash sweep accounts, U.S. Treasury money market mutual fund, bank certificates of deposit, U.S. Treasury bills and corporate bonds that have a maturity of three months or less from the original acquisition date.

The Company has classified assets measured at fair value on a recurring basis as follows as of December 31, 2019:

			Fair Value Measurement Based on		
	Amortized Cost	Fair Value	Quoted Prices in Active Market (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents (1)	$ 61,237	$ 61,237	$ 61,237	$ -	$ -
Corporate bonds	92,686	92,828	-	92,828	-
Total	$ 153,923	$ 154,065	$ 61,237	$ 92,828	$ -

(1) Includes cash sweep accounts, U.S. Treasury money market mutual fund, bank certificates of deposit, U.S. Treasury bills and corporate bonds that have a maturity of three months or less from the original acquisition date.

During the years ended December 31, 2020 and 2019, there were no transfers among the Level 1, Level 2 and Level 3 categories.

(Amounts in thousands, excluding share and per share items or as otherwise noted)

5. Property and Equipment

Property and equipment, net, consisted of:

	As of	
	December 31, 2020	December 31, 2019
Laboratory equipment	$ 8,566	$ 5,717
Computer hardware and equipment	109	105
Furniture and fixtures	432	396
Leasehold improvements	320	312
Construction in process	3,320	203
	12,747	6,733
Less: accumulated depreciation	(2,734)	(1,807)
	$ 10,013	$ 4,926

Depreciation expense was $1,592 and $862 for the years ended December 31, 2020 and 2019, respectively.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of:

	As of	
	December 31, 2020	December 31, 2019
Employee compensation and related benefits	$ 3,808	$ 2,816
Professional fees	224	300
Contract manufacturing organization fees	582	500
Contract research organization fees	487	182
University partnerships	183	448
Property received not yet invoiced	385	260
Other	723	544
	$ 6,392	$ 5,050

7. Commitments and Contingencies

Leases

The Company recognizes rent expense on a straight-line basis over the lease period and has accrued for rent expense incurred but not yet paid. Landlord allowances for tenant improvements are deferred and recognized as a reduction to rent expense on a straight-line basis and over the remaining lease term.

In March 2018, the Company entered into a lease for office and laboratory facilities that expires in July 2025. Under the terms of the lease, the Company placed $290 letter of credit into a restricted cash account as security for the facility.
In December 2018, the Company signed a collaboration agreement (the Collaboration Agreement) with Cell Therapy Catapult Limited (Catapult) to establish the Company's manufacturing process in Catapult's GMP manufacturing facility in the United Kingdom. The initial term of the Collaboration Agreement is three years which began March 1, 2019. The Company can terminate the Collaboration Agreement earlier with 12 months' notice and continued payment for contributions during the 12-month termination period.

The Collaboration Agreement provides for Catapult to provide identified space, called a module. The agreement calls for the Company to pay certain amounts for use of the module, operating, and overhead expenses. The Company has concluded that the Collaboration Agreement contains an embedded lease as the Company has the right to operate the module in a manner it determines. The Company also concluded that it is not the deemed owner during modification of the module nor does the agreement represent a capital lease under ASC 840, "Leases". As a result, the embedded lease portion of the Collaboration Agreement will be accounted for as an operating lease. The Company determined the amounts to be representative of rent to be £300 per year based on the relative selling prices of the services being provided. This amount will be amortized annually on a straight-line basis as rent expense over the term of the embedded lease, commencing March 1, 2019.

(Amounts in thousands, excluding share and per share items or as otherwise noted)

In September 2019, the Company entered into a lease for office facilities that expires in August 2024. Under the terms of the lease, the Company placed $127 letter of credit into a restricted cash account as security for the facility.

In November 2020, the Company entered into a lease for office and laboratory facilities that expires in December 2023. Under the terms of the lease, the Company placed $166 letter of credit into a restricted cash account as security for the facility.

In November 2020, the Company entered into a manufacturing agreement with Elevatebio which includes identified space dedicated to the Company. The Company has determined the agreement contains an embedded lease. The Company also concluded that it is not the deemed owner during modification of the module nor does the agreement represent a capital lease under ASC 840, “Leases”. As a result, the embedded lease portion of the Collaboration Agreement will be accounted for as an operating lease.

The following table presents future minimum rent payments under non-cancellable operating leases with initial terms in excess of one year at December 31, 2020:

	As of December 31, 2020
2021	$ 4,966
2022	3,985
2023	3,690
2024	2,537
2025	1,054
Thereafter	-
Total minimum payments required	$ 16,232

Litigation

The Company is not currently party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses as incurred the costs related to such legal proceedings.

Royalty transfer agreement

In connection with the sale of Series A redeemable convertible preferred stock (see Note 9), certain investors are entitled to receive, in the aggregate, a royalty from the Company equal to one percent of (i) all global net sales of any Company products and (ii) any license income on intellectual property that was in existence at the time of the Series A preferred stock financing. The Company has elected to account for this liability at fair value with changes recognized in the statement of operations. Given the early stage nature of the underlying technology and inherent risks associated with obtaining regulatory approval and achieving commercialization, the Company ascribed no value to the royalty agreement at inception and for the years ended December 31, 2020 and 2019. The Company currently does not have any net sales or license income and as a result has paid no royalties under this obligation as of December 31, 2020 and 2019 nor has the Company accrued any liability as of December 31, 2020 and 2019.

8. 401(k) Savings Plan

The Company maintains a defined contribution 401(k) plan in which employees may contribute a portion of their compensation, subject to statutory maximum contribution amounts. For the years ended December 31, 2020 and 2019, the matching contribution expense was $369 and $276, respectively.

9. Common Stock and Redeemable Convertible Preferred Stock

Common stock

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company’s stockholders. Subject to the rights of holders of redeemable convertible preferred stock, common stockholders are entitled to receive dividends, as may be declared by the Board of Directors, if any. No dividends had been declared through December 31, 2020.

Preferred stock

The Board of Directors or any authorized committee thereof is expressly authorized, to the fullest extent permitted by law, to provide by resolution or resolutions for, out of the unissued shares of Undesignated Preferred Stock, the issuance of the shares of Undesignated Preferred Stock in one or more series of such stock, and by filing a certificate of designations pursuant to applicable law of the State of Delaware, to establish or change from time to time the number of shares of each such series, and to fix the designations, powers, including voting powers, full or limited, or no voting powers, preferences and the relative, participating, optional or other special rights of the shares of each series and any qualifications, limitations and restrictions thereof. As of December 31, 2020, there are no preferred shares issued.

Redeemable Convertible Preferred Stock

Upon completion of the IPO during February 2019, all redeemable convertible preferred stock was converted to common stock.

Prior to the IPO, the Company elected to accrete the carrying value of the Series A and B preferred stock to redemption value at the end of each reporting period as if the end of the reporting period were the redemption date. Increases to the carrying value of redeemable convertible preferred stock are charged to additional paid-in capital or, in the absence of additional paid-in capital, charged to accumulated deficit.

Series A Redeemable Convertible Preferred Stock

Prior to the IPO, there were 44,500,001 Series A preferred shares issued and outstanding. Included in the Series A preferred stock purchase agreement, the investor is required to purchase additional shares upon the achievement of certain Company milestones. The Company evaluated the future commitment obligations at original issuance and determined they were not freestanding instruments as they were not legally detachable. The future commitment obligations were also evaluated as embedded derivatives and determined they did not meet the definition of a derivative instrument for which bifurcation would be required. The Series A preferred stock is classified outside of stockholders' equity (deficit) as the preferred holders may, at their option, elect to have their shares redeemed upon written notice by a majority of the preferred shareholders and at any time after February 2023.

Upon completion of the IPO in February 2019, all Series A preferred stock was converted to 7,184,588 shares of common stock.

Conversion

Prior to the IPO, each share of Series A preferred stock was convertible, at the option of the holder, into shares of common stock. Prior to the common stock reverse stock split in February 2019, the shares were convertible on a one-to-one basis. Post-split the Series A stock were convertible at 1-to-0.1615 basis. The Series A conversion rights were subject to adjustment for certain dilutive events. The conversion price could have been adjusted to prevent dilution of the Series A preferred stock.

The preferred stock was also mandatorily convertible upon the closing of an initial public offering resulting in gross proceeds to the Company exceeding $50,000 or by a written election by the majority of the Series A stockholders.

Redemption

Prior to the IPO, at the election of a majority of the Series A stockholders, the Series A preferred stock was redeemable at any time on or after October 16, 2020. The Series A preferred stock may be redeemed at a price equal to the greater of (a) the original issuance price, plus any cumulative dividends accrued but unpaid thereon, whether or not declared, or (b) the fair market value as of the date of the redemption.

Dividends

Prior to the IPO, the holders of shares of Series A preferred stock were entitled to receive cumulative dividends of 6% from the date of issuance. Accumulated dividends were payable only when and if declared by the Board of Directors, in preference to dividends paid to holders of common stock. The dividend preference for Series A preferred stock is $0.06 per share, as adjusted for recapitalizations. No dividends were declared prior to the IPO.

Liquidation

Prior to the IPO, in the event of a liquidation, dissolution or winding up of the Company, either voluntary or involuntary, or in the event of a deemed liquidation event, which included a sale of the Company as defined in the Company's certificate of incorporation, holders of Series A preferred stock were entitled to receive, subject to the preference of the Series B holders but in preference to common stockholders, an amount equal to their original investment amount plus any declared and unpaid dividends. If upon the occurrence of such event, the assets and funds available for distribution were insufficient to pay such holders the full amount to which they are entitled, then the entire assets and funds legally available for distribution would have been distributed ratably among the holders of the Series A preferred stock in proportion to the full amounts to which they would otherwise be entitled.

After payment of the liquidation preference on shares of Series A preferred stock had been made, any remaining assets would have been distributed ratably to common, Series B stockholders and Series A stockholders, on an as-converted basis.

Series B Redeemable Convertible Preferred Stock

Prior to the IPO, there were 62,500,000 Series B preferred shares issued and outstanding. The Series B preferred stock is classified outside of stockholders' equity (deficit) as the preferred holders may, at their option, elect to have their shares redeemed upon written notice by a majority of the preferred shareholders and at any time after February 2023.

Upon completion of the IPO in February 2019, all Series B preferred stock was converted to 10,090,711 shares of common stock.

Conversion

Prior to the IPO, each share of Series B preferred stock was convertible, at the option of the holder, into shares of common stock. Prior to the common stock reverse stock split in February 2019, the shares were convertible on a one-to-one basis. Post-split the Series B stock were convertible at 1-to-0.1615 basis. The Series B conversion rights were subject to adjustment for certain dilutive events. The conversion price could have been adjusted to prevent dilution of the Series B preferred stock.

The Series B preferred stock was also mandatorily convertible upon the closing of an initial public offering resulting in gross proceeds to the Company exceeding $50,000 or by a written election by the majority of the Series B stockholders.

Redemption

Prior to the IPO, at the election of a majority of the Series B stockholders, the Series B preferred stock was redeemable at any time on or after February 2023. The Series B preferred stock could have been redeemable at a price equal to the greater of (a) the original issuance price, plus any cumulative dividends accrued but unpaid thereon, whether or not declared, or (b) the fair market value as of the date of the redemption.

Dividends

Prior to the IPO, the holders of shares of Series B preferred stock were entitled to receive cumulative dividends of 6% from the date of issuance. Accumulated dividends were payable only when and if declared by the Board of Directors, in preference to dividends paid to holders of Series B preferred stock and common stock. The dividend preference for Series B preferred stock was $0.12 per share, as adjusted for recapitalizations. No dividends were declared prior to the IPO.

Liquidation

Prior to the IPO, in the event of a liquidation, dissolution or winding up of the Company, either voluntary or involuntary, or in the event of a deemed liquidation event, which includes a sale of the Company as defined in the Company's articles of incorporation, holders of Series B preferred stock were entitled to receive, in preference to the holders of Series A preferred stock or common stock, an amount equal to their original investment amount plus any declared and unpaid dividends. If upon the occurrence of such event, the assets and funds available for distribution were insufficient to pay such holders the full amount to which they are entitled, then the entire assets and funds legally available for distribution would have been distributed ratably among the holders of the Series B preferred stock in proportion to the full amounts to which they would otherwise be entitled.

After payment of the liquidation preference on shares of Series B preferred stock has been made, any remaining assets would have been distributed ratably to Series A stockholders in an amount equal to their original investment amount plus any accrued dividends,

(Amounts in thousands, excluding share and per share items or as otherwise noted)

whether or not declared, together with any other dividends declared but unpaid thereon. After payment of the liquidation preference on shares of Series A preferred stock had been made, any remaining assets would have been distributed ratably to common, Series B stockholders and Series A stockholders, on an as-converted basis.

10. Stock-based Compensation

In February 2019, the Company's Board of Directors and stockholders approved the 2018 Stock Option and Incentive Plan (the 2018 Plan), which replaced the 2015 Plan. The shares under the 2015 Plan which were not issued, were rolled into the 2018 Plan. The number of shares of our common stock reserved for issuance under the 2018 Plan shall be cumulatively increased on January 1, 2020 and each January 1 thereafter by 4% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year or a lesser number of shares determined by our Board of Directors.

The 2018 Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. The Company's officers, employees, directors and other key persons (including consultants) are eligible to receive awards under the 2018 Plan. The amount, terms of grants, and exercisability provisions are determined and set by the Company's Board of Directors. The maximum number of authorized shares to be issued under the Plan was 6,053,935. As of December 31, 2020, there were 700,294 shares of common stock available for future issuance. The term of the options may be up to 10 years, and options are exercisable in cash or as otherwise determined by the Board of Directors. Generally, options and restricted stock awards vest over a four -year period.

The Company recorded stock-based compensation expense in the following expense categories of its accompanying consolidated statements of operations:

	For the Years Ended December 31,	
	2020	2019
Research and development	$ 3,351	$ 2,547
General and administrative	5,141	4,155
	$ 8,492	$ 6,702

Stock options

The following table summarizes the activity related to stock option grants to employees and non-employees for the years ended December 31, 2020 and 2019:

	Shares	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Life (in Years)
Balance at January 1, 2019	2,121,561	$ 3.78	9.1
Granted	2,287,889	15.78	
Exercised	(100,421)	2.55	
Forfeited	(119,737)	5.60	
Balance at December 31, 2019	4,189,292	$ 10.31	8.9
Granted	1,252,365	28.12	
Exercised	(241,995)	3.91	
Forfeited	(188,313)	12.31	
Balance at December 31, 2020	5,011,349	$ 14.99	8.4
Exercisable at December 31, 2020	1,848,628	8.18	7.5
Vested and expected to vest at December 31, 2020	5,011,349		

The above table excludes 8,017 options that were granted outside of the Plan.

As of December 31, 2020, there was $37,383 in unrecognized compensation cost that is expected to be recognized over an estimated weighted-average amortization period of 3.2 years. The aggregate intrinsic value of options outstanding and options exercisable as of December 31, 2020 was $42,068. The aggregate intrinsic values of options exercised during the year ended December 31, 2020 was $3,908.

(Amounts in thousands, excluding share and per share items or as otherwise noted)

The fair value of options is estimated using the Black-Scholes option pricing model, which takes into account inputs such as the exercise price, the value of the underlying common stock at the grant date, expected term, expected volatility, risk-free interest rate and dividend yield. The fair value of each grant of options during the years ended December 31, 2020 and 2019 was determined using the methods and assumptions discussed below:

- The expected term of employee options is determined using the “simplified” method, as prescribed in the SEC Staff Accounting Bulletin (SAB) No. 107, whereby the expected life equals the arithmetic average of the vesting term and the original contractual term of the option due to the Company’s lack of sufficient historical data. The expected term of non-employee options is equal to the contractual term.
- The expected volatility is based on historical volatilities of similar entities within the Company’s industry which were commensurate with the expected term assumption as described in SAB No. 107.
- The estimated annual dividend yield is 0% because the Company has not historically paid, and does not expect for the foreseeable future to pay, a dividend on its common stock.
- Post IPO, the company is traded on the Nasdaq Select Market. Fair value is determined by the stock price quoted on the Nasdaq. Prior to the IPO, the Company considered numerous objective and subjective factors in estimating the fair value of its common stock, including the estimated fair value of the Company’s Series A and Series B preferred stock.

For the years ended December 31, 2020 and 2019, the grant date fair value of all option grants was estimated at the time of grant using the Black-Scholes option-pricing model using the following weighted average assumptions:

	For the Years Ended December 31,	
	2020	2019
Risk-free interest rate	0.5%	2.08%
Expected term (in years)	6.1	6.0
Expected volatility	75.0%	70.4%
Annual dividend yield	0%	0%
Fair value of common stock	$ 18.51	$ 10.06

Warrants

Warrants issued to non-employees in connection with providing consulting services are issued outside of the Plan and are accounted for as stock-based compensation.

The warrants have an initial exercise price of $0.74 per share and will expire at the earlier of ten years from the date of issuance or a change in control event as defined in the warrant agreements.

As of December 31, 2020 and 2019, there were 203,676 warrants outstanding. During the years ending December 31, 2020 and 2019, the Company granted no warrants and there were no forfeitures.

Employee stock purchase plan (ESPP)

In February 2019, the Company’s Board of Directors adopted and the Company’s stockholders approved the 2018 Employee Stock Purchase Plan (2018 ESPP). The 2018 ESPP enables eligible employees to purchase shares of the Company's common stock at the end of each six-month offering period at a price equal to 85% of the fair market value of the shares on the first business day or the last business day of the offering period, whichever is lower. Eligible employees generally included all employees. Offering periods began on the first trading day September 1 and March 1 of each year and ended on the last trading day in February and August of each year. Share purchases are funded through payroll deductions of up to 15% of an employee’s eligible compensation for each payroll period, or $25 each calendar year.

During the years ended December 31, 2020 and 2019, there were 23,864 and 10,614 shares issued under the 2018 ESPP, respectively.

(Amounts in thousands, excluding share and per share items or as otherwise noted)

11. Income tax expense

Loss before income tax expense for the years ended December 31, 2020 and 2019 consisted of the following:

	For the Years Ended December 31,	
	2020	2019
United States	$ (67,625)	$ (47,960)
Foreign	662	463
Loss before income taxes	$ (66,963)	$ (47,497)

The income tax expense for the years ended December 31, 2020 and 2019 consisted of the following components:

	For the Years Ended December 31,	
	2020	2019
Current tax		
State	$ 30	$ 40
Total current tax	30	40
Deferred tax		
Foreign	131	62
Total deferred tax	131	62
Income tax expense	$ 161	$ 102

Subject to the limitations described below, at December 31, 2020, we have cumulative federal and state net operating loss carryforwards of approximately $4.1 million and $129.0 million available to reduce federal and state taxable income, respectively, which begin to expire in 2035. Additionally, we have $122.3 million of federal net operating loss carryforwards which carryforward indefinitely. We have cumulative federal and state tax credit carry forwards of $5.6 million and $2.4 million, respectively, available to reduce federal and state income taxes which begin to expire in 2035 and 2031, respectively.

Section 382 of the Internal Revenue Code of 1986, as amended (the Code) provides for limitation on the use of net operating loss and research and development tax credit carryforwards following certain ownership changes (as defined in Code) that could limit the Company's ability to utilize these carryforwards. Pursuant to Section 382 of the Code, an ownership change occurs when the stock ownership of a 5% stockholder increases by more than 50% over a three-year testing period. The Company may have experienced various ownership changes, as defined by the Code, as a result of past financings and may in the future experience an ownership change. Accordingly, the Company's ability to utilize the aforementioned carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be applied against future taxes. The Company has not performed an Internal Revenue Code Section 382 study in connection with changes in control.

The components of net deferred income tax assets (liabilities) as of December 31, 2020 and 2019 are as follows:

	As of December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 34,749	$ 17,120
Research and development credits	7,584	4,814
Capitalized costs	5,646	6,234
Accrued expenses and other	1,020	907
Stock compensation	2,874	1,311
Total deferred tax assets	51,873	30,386
Deferred tax liabilities:		
Depreciation	(392)	(171)
Total deferred tax liabilities	(392)	(171)
Less: valuation allowance	(51,683)	(30,277)
Total net deferred tax assets (liabilities)	$ (202)	$ (62)

In assessing the realizability of the net deferred tax assets, the Company considers all relevant positive and negative evidence in determining whether it is more likely than not that some portion or all of the deferred income tax assets will not be realized. The realization of the gross deferred tax assets is dependent on several factors, including the generation of sufficient taxable income prior to the expiration of the net operating loss carryforwards. Management believes that it is more likely than not that the Company's U.S. deferred income tax assets will not be realized. As such, there is a full valuation allowance against the net U.S. deferred tax assets as of December 31, 2020 and 2019. The Company is in a net deferred tax liability position in the United Kingdom and believes it is more likely than not that the foreign deferred income tax assets will be realized. As such, there is no

(Amounts in thousands, excluding share and per share items or as otherwise noted)

valuation allowance against the U.K. deferred tax assets. The valuation allowance in the U.S. increased by approximately $21.4 million during the year ended December 31, 2020 primarily as a result of the increase in net operating loss carryforwards. The valuation allowance increased by approximately $15.8 million during the year ended December 31, 2019 primarily as a result of the increase in net operating loss carryforwards.

The Company did not have unrecognized tax benefits as of December 31, 2020 or 2019. The Company recognizes interest and penalties accrued on any unrecognized tax benefits as a component of income tax expense.

A reconciliation of income tax expense at the statutory federal income tax rate and income taxes as reflected in the financial statements is as follows:

	As of December 31,	
	2020	2019
Statutory Federal income tax rate	21.0%	21.0%
State income tax, net of federal benefit	6.4%	6.4%
Permanent differences	0.1%	-0.4%
Research and development credit benefit	4.1%	5.9%
Change in valuation allowance	-32.0%	-33.1%
Effective income tax rate	-0.4%	-0.2%

The Company's remains subject to examination by U.S. Federal, state, local, and foreign tax authorities for tax years 2017 through 2020. With a few exceptions, we are no longer subject to U.S. Federal, state, local, and foreign examinations by tax authorities for the tax year 2016 and prior. However, net operating losses from the tax year 2016 and prior would be subject to examination if and when used in a future tax return to offset taxable income.

Management believes that the Company does not have any uncertain tax positions that would result in a material impact on the Company's financial statements. The Company files income tax returns in the above jurisdictions as well as the applicable state jurisdictions in the United States. There are currently no income tax examinations ongoing. If and when applicable, the Company will recognize interest and penalties on uncertain tax positions as income tax expense.

12. Related party transactions

Manufacturing agreement

During November 2020, we entered into a manufacturing partnership with ElevateBio, LLC. Dr. Ansbert Gadicke is a member of the board of directors at the Company and ElevateBio, LLC. The agreement is to establish a manufacturing partnership with ElevateBio, LLC for production of the Company's clinical trial products. During the year ended December 31, 2020, we incurred $760 in expenses and have incurred additional costs of $1,600 for equipment owned by us for use by ElevateBio, LLC.

Consulting arrangements

On October 1, 2015, we entered into a consulting agreement with Dr. Patrick Baeuerle. Pursuant to the consulting agreement, Dr. Baeuerle agreed to perform such consulting, advisory and related services to and for us as may be reasonably requested. In exchange, we agreed to pay Dr. Baeuerle a consulting fee of €15 per month. On November 1, 2016, we amended the consulting agreement to revise Dr. Baeuerle's consulting fee to be €3 per month. Dr. Baeuerle is also eligible for an annual bonus equal to 33% of the annual fees paid under the consulting agreement, subject to the discretion of our Board of Directors based on Dr. Baeuerle's performance and our performance. The term of the agreement is one year, and automatically extends for additional one-year periods unless terminated. During the years ended December 31, 2020 and 2019, we incurred fees and travel related expenses to Dr. Baeuerle in the amount of $74 and $72, respectively, under the consulting agreement. Dr. Baeuerle is a member of our Board of Directors and is a managing director at MPM Capital, the beneficial owner of more than 5% of our voting securities.

On March 2, 2016, the Company entered into a consulting agreement with Dr. Mitchell Finer (the Original Finer Agreement), which was amended and restated on May 9, 2017 to, among other things, add Pattern Recognition Ventures as a party. Pursuant to the amended and restated consulting agreement, Pattern Recognition Ventures agreed to perform scientific consulting, advisory and related services to and for the Company as may be reasonably requested, including making Dr. Finer available to serve as Chairman of the Company's Scientific Advisory Board. Pursuant to the amended and restated consulting agreement, the Company agreed to pay Pattern Recognition Ventures a consulting fee of $19 per quarter for services provided under the agreement, commencing on July 1, 2017. On June 5, 2020, the Company and Pattern Recognition Ventures amended the agreement to provide for consulting fees of $100 per year.

Dr. Finer was a member of the Board of Directors from 2015 until his resignation on April 30, 2020. Dr. Finer is not considered a related party after his resignation from the Board of Directors. During the twelve months ended December 31, 2020 and 2019, the Company incurred fees and travel-related expenses to Pattern Recognition Ventures in the amount of $19 and $77, respectively. Dr. Finer has a financial interest in Pattern Recognition Ventures and is its managing member. Dr. Finer is an executive partner at MPM Capital, the beneficial owner of more than 5% of the Company's voting securities.

13. Subsequent Event

On January 19, 2021, TCR2 Therapeutics Inc., a Delaware corporation entered into an underwriting agreement with Goldman Sachs & Co. LLC, Jefferies LLC, Piper Sandler & Co. and BMO Capital Markets Corp., related to the public offering of 4,590,164 shares (the “Shares”) of the Company’s common stock, par value $0.0001 per share (the “Common Stock”), at a price to the public of $30.50 per Share, less underwriting discounts and commissions. The offering was made pursuant to the Company’s shelf registration statement on Form S-3 (File No. 333-236965), including a base prospectus that was declared effective by the U.S. Securities and Exchange Commission (the “SEC”) on April 28, 2020, as supplemented by a prospectus supplement dated January 19, 2021 that was filed with the SEC on January 21, 2021. The offering closed on January 22, 2021. The Company received net proceeds from the offering, after deducting the underwriting discounts and commissions and other estimated offering expenses payable by the Company, of approximately $131.1 million.

(Amounts in thousands, excluding share and per share items or as otherwise noted)

14. Quarterly Financial Information (unaudited)

	Three Months Ended			
	December 31, 2020	September 30, 2020	June 30, 2020	March 31, 2020
Operating expenses				
Research and development	$ 14,298	$ 12,820	$ 12,907	$ 11,955
General and administrative	4,269	4,371	3,809	4,271
Total operating expenses	18,567	17,191	16,716	16,226
Loss from operations	(18,567)	(17,191)	(16,716)	(16,226)
Interest income, net	191	300	499	747
Loss before income tax expense	(18,376)	(16,891)	(16,217)	(15,479)
Income tax expense	75	31	28	27
Net loss	$ (18,451)	$ (16,922)	$ (16,245)	$ (15,506)
Per share information				
Net loss per share of common stock, basic and diluted	$ (0.55)	$ (0.56)	$ (0.67)	$ (0.65)
Weighted average shares outstanding, basic and diluted	33,448,315	30,340,355	24,075,984	24,011,843

	Three Months Ended			
	December 31, 2019	September 30, 2019	June 30, 2019	March 31, 2019
Operating expenses				
Research and development	$ 9,392	$ 11,374	$ 8,833	$ 7,889
General and administrative	4,179	3,522	3,307	2,886
Total operating expenses	13,571	14,896	12,140	10,775
Loss from operations	(13,571)	(14,896)	(12,140)	(10,775)
Interest income, net	846	1,090	1,077	872
Loss before income tax expense	(12,725)	(13,806)	(11,063)	(9,903)
Income tax expense	102	-	-	-
Net loss	(12,827)	(13,806)	(11,063)	(9,903)
Accretion of redeemable convertible preferred stock to redemption value	-	-	-	(49,900)
Net loss attributable to common stockholders	$ (12,827)	$ (13,806)	$ (11,063)	$ (59,803)
Per share information				
Net loss per share of common stock, basic and diluted	$ (0.54)	$ (0.58)	$ (0.46)	$ (4.85)
Weighted average shares outstanding, basic and diluted	23,961,960	23,874,593	23,818,003	12,328,805

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 or financial disclosure required to be reported under this Item.

Item 9A. Controls and Procedures

Disclosure Controls and Procedures

The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the Exchange Act), refers to controls and procedures that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that such information is accumulated and communicated to a company’s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

In designing and evaluating our disclosure controls and procedures, management recognizes that disclosure controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the disclosure controls and procedures are met. Additionally, in designing disclosure controls and procedures, our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible disclosure controls and procedures. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a control system, misstatements due to error or fraud may occur and not be detected.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2020. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of the end of the period covered by this report at the reasonable assurance level.

Changes in Internal Control over Financial Reporting:

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended December 31, 2020 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management’s Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company’s principal executive and principal financial officers and effected by the company’s Board of Directors, management and other personnel, 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 and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company’s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2020. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission

in *Internal Control—Integrated Framework* (2013 framework) (COSO). Based on its assessment, management concludes that, as of December 31, 2020, our internal control over financial reporting is effective based on those criteria.

Item 9B. Other Information

On March 15, 2021, our Board of Directors approved Amendment No. 1 (the "Amendment") to our Amended and Restated By-Laws (the "Amended and Restated By-Laws"), which became effective as of the same date. The Amendment updates our exclusive forum provision for Securities Act claims.

The foregoing description of the Amendment is qualified in its entirety by reference to the full text of the Amendment, a copy of which is filed as Exhibit 3.3 to this Annual Report on Form 10-K and incorporated by reference herein.

Part III

Item 10. Directors, Executive Officers and Corporate Governance

The following table sets forth information about our directors, executive officers and other key employees as of March 1, 2021.

Name	Age	Position
Executive Officers		
Garry E. Menzel	56	President, Chief Executive Officer and Director
Robert Hofmeister	53	Chief Scientific Officer
Angela Justice	48	Chief People Officer
Alfonso Quintas Cardama	50	Chief Medical Officer
Mayur (Ian) Somaiya	47	Chief Financial Officer
Non-Employee Directors		
Ansbert Gadicke (3)(4)	63	Chairman of the Board of Directors
Andrew Allen (1)(2)(4)	54	Director
Patrick Baeuerle	63	Director
Neil W. Gibson (1)(2)	64	Director
Axel Hoos(3)	51	Director
Shawn Tomasello (2)(3)	62	Director
Stephen Webster (1)(4)	59	Director

(1) Member of audit committee

(2) Member of compensation committee

(3) Member of nominating and corporate governance committee

(4) Member of finance and strategy committee

Executive Officers

Garry Menzel, Ph.D. Dr. Menzel joined our company in 2016 as a director and Chief Executive Officer. Dr. Menzel has also served on the board of directors and chairman of the audit committee of the oncology company Black Diamond Therapeutics Inc. since 2014 and has served on the board of directors of Stoke Therapeutics Inc. since 2020. Previously, Dr. Menzel was the Chief Strategy Officer at Axcella Health Inc. from 2015 to 2016, the Chief Financial Officer at DaVita Healthcare Partners Inc. from 2013 to 2015, and the Chief Operating Officer at Regulus Therapeutics Inc. from 2008 to 2013. Dr. Menzel also had global leadership roles in running the biotechnology practices at Goldman Sachs & Co. LLC from 1994 to 2004 and Credit Suisse Group AG from 2004 to 2008. In addition, he was a consultant with Bain & Company and was a research assistant at SmithKline Beecham PLC (now GlaxoSmithKline PLC). Dr. Menzel received his Ph.D. from the University of Cambridge, where he studied the regulation of oncogenes in immune cells, and his M.B.A. from the Stanford University Graduate School of Business. We believe Dr. Menzel is qualified to serve as a member of our board of directors because of his scientific background and corporate leadership experience.

Robert Hofmeister, Ph.D. Dr. Hofmeister joined our company in September 2015 as Senior Vice President, Research and Development and became our Chief Scientific Officer in October 2016. From 2005 to 2015, Dr. Hofmeister held positions at EMD Serono Research and Development Institute, Inc., including as the Global Head of Translational Immunotherapy, Immuno-Oncology from 2012 to 2015. Previously, Dr. Hofmeister held positions at Micromet AG (now a part of Amgen, Inc.). Dr. Hofmeister received his Ph.D. from the University of Regensburg in Germany, where he studied the signaling of the cytokine interleukin-1.

Angela Justice, Ph.D. Dr. Justice joined our company in October 2019 as Chief People Officer. From March 2018 to July 2019, Dr. Justice was the Chief Human Resources Officer at Surgery Partners, Inc. From 2012 to February 2018, Dr. Justice held several positions at Biogen, Inc., including serving as Chief Learning Officer from April 2015 to February 2018 and Senior Director of Global Medical Affairs for Biogen from 2012 to 2015. Dr. Justice received her B.S. from Minnesota State University at Mankato and her Ph.D. from the University of Chicago.

Alfonso Quintás Cardama, M.D. Dr. Quintás joined our company in 2017 as Chief Medical Officer. Dr. Quintás was the Clinical Development Head of the Cell & Gene Therapies Unit at GlaxoSmithKline PLC in 2017. Between 2014 and 2016, he served as Global Clinical Leader, Cell & Gene Therapy, at Novartis AG and was an Assistant Professor in the Department of Leukemia at The University of Texas, MD Anderson Cancer Center from 2009 to 2014. Dr. Quintás received his M.D. from the Universidad de Santiago de Compostela School of Medicine in Spain. He completed an internship and residency in the Department of Medicine of the Albert Einstein College of Medicine—Yeshiva University and a hematology and oncology fellowship and a leukemia fellowship at The University of Texas, MD Anderson Cancer Center.

Mayur (Ian) Somaiya. Mr. Somaiya joined our company in 2018 as Chief Financial Officer. From 2015 to 2018, Mr. Somaiya was Managing Director and Head of Biotechnology Research at BMO Capital Markets Corp. Previously, he served as a Managing

Director and Equity Analyst at Nomura Securities Co. Ltd. from 2013 to 2015, Piper Jaffray Companies from 2009 to 2013, Thomas Weisel Partners Group, Inc. from 2003 to 2009 and Morgan Stanley from 2000 to 2003. Mr. Somaiya received his B.A in Biology from New York University.

Non-Employee Directors

Ansbert Gadicke, M.D. Dr. Gadicke joined our board of directors in May 2015. Dr. Gadicke co-founded MPM Capital's venture investing activities in 1997 and has since served as a Managing Director. Prior to that, Dr. Gadicke led MPM Capital's Advisory and Investment Banking business from 1992 to 1996 and was in Boston Consulting Group's Health Care Group from 1989 to 1992. He is a member of the board of directors of Cullinan Oncology, LLC and ElevateBio, LLC and formerly served as a member of the board of directors of Radius Health, Inc. and Chiasma, Inc. Dr. Gadicke received his M.D. from J.W. Goethe University and has held research positions at the Whitehead Institute and Harvard University. We believe Dr. Gadicke is qualified to serve as a member of our board of directors because of his extensive experience in the life sciences industry and in investment management.

Andrew Allen, M.D., Ph.D. Dr. Allen joined our board of directors in December 2018. Dr. Allen is a co-founder of Gritstone Oncology, Inc., and has served as its President and Chief Executive Officer since August 2015. Dr. Allen previously co-founded Clovis Oncology, Inc., a public pharmaceutical development company, and served as its executive vice president of clinical and preclinical development and chief medical officer from April 2009 to July 2015. Prior to that, he was chief medical officer at Pharmion Corporation from 2006 to 2008. Previously, Dr. Allen served in clinical development leadership roles at Chiron Corporation and Abbott Laboratories, and worked at McKinsey & Company, where he advised life science companies on strategic issues. He currently serves on the board of directors of Gritstone Oncology, Inc., Epizyme, Inc., Sierra Oncology, Inc., and Revitope Oncology, Inc. Dr. Allen previously served on the board of directors of Cell Design Labs, a private biotechnology company, from November 2015 until its acquisition by Gilead Sciences, Inc. in December 2017. Dr. Allen qualified in medicine at Oxford University and received a Ph.D. in immunology from Imperial College of Science, Technology and Medicine in London. We believe Dr. Allen is qualified to serve on our board of directors due to his educational experience and his experience as a founder and senior executive of biotechnology and pharmaceutical companies.

Patrick Baeuerle, Ph.D. Dr. Baeuerle has served on our board of directors since May 2015. Since 2015, Dr. Baeuerle has been a Managing Director of MPM Capital. From 2012 to 2015 he served as Vice President, Research, and General Manager at Amgen Research (Munich) GmbH. From 1998 to 2012, Dr. Baeuerle served as Chief Scientific Officer for Micromet, Inc. Dr. Baeuerle co-founded Harpoon Therapeutics, Inc. in 2015. Dr. Baeuerle also co-founded Cullinan Oncology, LLC, of which he is Chief Scientific Officer—Biologics, Maverick Therapeutics, Inc. and iOmx AG. He currently serves on the board of directors of Harpoon Therapeutics and the advisory boards of Amphivena Therapeutics, Inc., iOmx AG and Maverick Therapeutics, Inc. He is also an Honorary Professor of Immunology of the Medical Faculty at University of Munich. Dr. Baeuerle received his Ph.D. in biology from the University of Munich and performed post-doctoral research at the Whitehead Institute. We believe Dr. Baeuerle is qualified to serve as a member of our board of directors because of his scientific background, experience in the venture capital industry, corporate leadership experience and his experience as a founder of numerous biopharmaceutical companies.

Axel Hoos, MD, Ph.D. Dr. Axel Hoos is Senior Vice President, R&D Governance Chair, and Therapeutic Area Head for Oncology at GlaxoSmithKline Pharmaceuticals (GSK). As R&D Governance Chair he oversees technical and funding review committees. As Therapeutic Area Head he is responsible for the Oncology business including discovery and development with the four focus areas of immuno-oncology, epigenetics, cell & gene therapy and synthetic lethality. He has also been responsible for leading business development portfolio expansions including the acquisition of Tesaro and the cell & gene therapy licensing agreements with Adaptimmune, Lyell and Immatics. Dr. Hoos also serves as Chairman of the Board of Trustees of the Sabin Vaccine Institute, is Co-founder and Director on the Board of Imugene, a biotech company, Co-Director of the Cancer Immunotherapy Consortium and Scientific Advisory Board Member of the Cancer Research Institute. Prior to GSK, Dr. Hoos was the Global Medical Lead in Immunology/Oncology at Bristol-Myers Squibb where he developed Yervoy (Ipilimumab) which was the first checkpoint inhibitor drug in immuno-oncology. The discovery of ipilimumab's scientific mechanism was honored with the Nobel Prize for Physiology or Medicine to Dr. James Allison in 2018. Dr. Hoos was also Senior Director of Clinical Development at Agenus Bio. Dr. Hoos holds an MD from Ruprecht-Karls-University and a PhD in molecular oncology from the German Cancer Research Center (DKFZ). He trained in surgery at the Technical University in Munich and at Memorial Sloan-Kettering Cancer Center in New York City (where he also studied molecular pathology and tumor immunology). He is an alumnus of the Program for Leadership Development at Harvard Business School.

Neil Gibson, Ph.D. Dr. Gibson has served on our board of directors since February 2018. Since 2016, he has served as Senior Vice President to COI Pharmaceuticals, Inc. and President and CEO of PDI Therapeutics. From 2015 to 2016, Dr. Gibson served as Senior Vice President and Chief Development Officer to BioAtla LLC. From 2011 to 2015, he served as Chief Scientific Officer of Regulus Therapeutics Inc., and from 2007 to 2011 he was Chief Scientific Officer of Pfizer Oncology based in La Jolla, CA. Dr. Gibson received his Ph.D. from the University of Aston and his B.Sc. from the University of Strathclyde. We believe Dr. Gibson is qualified to serve on our board of directors because of his extensive experience in the life sciences industry.

Shawn Tomasello. Ms. Tomasello served as the Chief Commercial Officer of Kite Pharma, where she oversaw the global commercialization of Yescarta, from 2015 to 2018 including through its acquisition by Gilead for $11.9 billion in October 2017. She was previously Chief Commercial Officer at Pharmacyclics, where she led commercial and medical affairs activities for Imbruvica®, a first-in-class treatment for hematologic malignancies, from August 2014 until its acquisition by AbbVie for $21.0 billion in August 2015. Prior to Pharmacyclics, Ms. Tomasello served in leading commercial roles with multiple major pharmaceutical companies, including Celgene as President of the Americas Hematology and Oncology, where she led the company through five successful product launches encompassing 11 indications and played a critical role in acquisitions. Ms. Tomasello received her B.S. in Marketing from the University of Cincinnati and her M.B.A. from Murray State University in Kentucky.

Stephen Webster. Mr. Webster served as the Chief Financial Officer of Spark Therapeutics, a publicly traded gene therapy biotechnology company, from July 2014 until its acquisition by Roche for $4.8 billion in December 2019. He was previously Senior Vice President (SVP) and Chief Financial Officer of Optimer Pharmaceuticals, a publicly traded biotechnology company, from July 2012 until its acquisition by Cubist Pharmaceuticals in October 2013. Prior to joining Optimer, Mr. Webster served as SVP and Chief Financial Officer of Adolor Corporation, a biopharmaceutical company, from 2008 until its acquisition by Cubist Pharmaceuticals in 2011. Mr. Webster also served in leadership positions in the investment banking healthcare groups of Broadpoint Capital and PaineWebber Incorporated. Mr. Webster has served as a director of NextCure, a publicly traded biopharmaceutical company, since April 2019, Nabriva Therapeutics AG (formerly Nabriva Therapeutics plc), a publicly traded biopharmaceutical company, since August 2016 and Viking Therapeutics, a publicly traded biopharmaceutical company, since May 2014. Mr. Webster received an A.B. in Economics from Dartmouth College and an M.B.A. in Finance from The Wharton School of the University of Pennsylvania.

Family Relationships

There are no family relationships among any of our directors or executive officers.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires our directors, executive officers and beneficial owners of more than 10% of our equity securities to file reports of holdings and transactions in securities of the Company with the SEC.

Based solely on a review of on Forms 3, 4 and 5 and any amendments thereto filed electronically with the Securities and Exchange Commission with respect to the most recent fiscal year and written representations from the reporting persons, we believe all Section 16(a) filing requirements were satisfied in 2020 with the exception of the following inadvertent late filing: a Form 4 filing filed on March 27, 2020 by Neil Gibson with respect to six transactions by Curative Ventures CT LLC.

Code of Business Conduct and Ethics

Our board of directors has adopted a Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics applies to all of our employees, officers (including our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions), agents and representatives, including directors and consultants.

The full text of our Code of Business Conduct and Ethics is posted on our website at www.tcr2.com. We intend to disclose future amendments to certain provisions of our Code of Business Conduct and Ethics on our website. The inclusion of our website address in this Annual Report does not include or incorporate by reference the information on our website into this Annual Report, and you should not consider that information a part of this Annual Report.

Audit Committee

The members of our audit committee are Andrew Allen, Neil Gibson and Stephen Webster. Stephen Webster is the chair of the audit committee. Our board of directors has determined that all members of our audit committee will meet the requirements for financial literacy under the applicable rules and regulations of the SEC and the Nasdaq listing rules and that Stephen Webster is an “audit committee financial expert” (within the meaning of applicable SEC regulations). Each of the members of the audit committee are independent pursuant to applicable Nasdaq listing standards.

Recommendation of Director Nominees by Stockholders

There have been no material changes to the procedures by which our stockholders may recommend nominees to the board of directors.

Item 11. Executive Compensation

Executive Compensation Overview

As an emerging growth company, we have opted to comply with the executive compensation disclosure rules applicable to "smaller reporting companies," as such term is defined in the rules promulgated under the Securities Act. This section provides an overview of the compensation awarded to and earned by each individual who served as our principal executive officer at any time during our years ended December 31, 2020 and 2019 and to our next two most highly compensated executive officers in respect of their service to our company for our years ended December 31, 2020 and 2019. We refer to these individuals as our named executive officers. Our named executive officers are:

- Garry Menzel, our President and Chief Executive Officer;
- Alfonso Quintás Cardama, our Chief Medical Officer;
- Mayur (Ian) Somaiya, our Chief Financial Officer.

Our executive compensation program is based on a pay-for-performance philosophy. Compensation for our executive officers is composed primarily of the following main components: base salary, bonus and equity incentives in the form of stock options. Our executive officers, like all full-time employees, are eligible to participate in our health and welfare benefit plans. As we transition from a private company to a publicly traded company, we intend to evaluate our compensation values and philosophy and compensation plans and arrangements as circumstances require.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to and earned by our named executive officers for services rendered to us in all capacities during our years ended December 31, 2020 and 2019.

NAME AND PRINCIPAL POSITION	YEAR	SALARY	OPTION AWARDS (1)	NON-EQUITY PLAN COMPENSATION (2)	ALL OTHER COMPENSATION	TOTAL
Garry Menzel, President and Chief Executive Officer	2020	$ 560,000	$ 5,196,450	$ 372,680	$ 8,550	$ 6,137,680
	2019	491,981	7,706,831	275,000	8,400	8,482,212
Alfonso Quintás Cardama, Chief Medical Officer	2020	451,500	2,142,210	218,526	8,550	2,820,786
	2019	421,561	3,335,108	165,500	8,400	3,930,569
Mayur (Ian) Somaiya, Chief Financial Officer	2020	393,750	1,951,320	190,575	8,550	2,544,195
	2019	368,750	2,372,239	144,375	10,781	2,896,145

(1) The amounts reported in the "Option Awards" column reflects the aggregate grant date fair value of share-based compensation awarded during the indicated year computed in accordance with the provisions of Financial Accounting Standards Board ASC Topic 718. See Note 10 to our consolidated financial statements appearing elsewhere in this Annual Report regarding assumptions underlying the valuation of equity awards.

(2) The amounts reported reflect annual bonuses earned based upon achievement of company and individual performance metrics. Amounts reflected are paid in the year subsequent to the performance year.

(3) Other compensation consists of the following:

		401(k) Matching Contribution	Moving Reimbursement	Total
Mayur (Ian) Somaiya, Chief Financial Officer	2019	8,400	2,381	10,781

Narrative to the Summary Compensation Table

Base Salary

We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. Base salaries are reviewed annually, typically in connection with our annual performance review process, and adjusted from time to time to realign salaries with market levels after taking into account individual responsibilities, performance and experience.

Annual Bonus

We have a formal performance-based bonus plan. Our employment arrangements with our named executive officers provide that the executive may be eligible to earn an annual performance bonus of up to a target percentage of the executive's base salary, as described further below under the section entitled "—Employment Arrangements and Severance Agreements with our Named Executive Officers". From time to time, our board of directors or compensation committee may approve additional annual bonuses

for our named executive officers based on individual performance, company performance or as otherwise determined to be appropriate. We have also adopted a senior executive cash bonus plan.

Equity Compensation

Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executive officers with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executive officers and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incentives our executive officers to remain in our employment during the vesting period. Accordingly, our board of directors periodically reviews the equity incentive compensation of our executives, including our named executive officers, and from time to time may grant equity incentive awards to them in the form of stock options.

We typically grant stock option awards at the start of employment to each executive officer and our other employees as well as on an annual basis for retention purposes. We award our stock options on the date our board of directors approves the grant. We set the option exercise price equal to the fair market value of our common stock on the date of grant.

401(k) Plan

We maintain a tax-qualified retirement plan (the 401(k) Plan) that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees are able to defer eligible compensation subject to applicable annual Code limits. Employees' pre-tax or Roth contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participants' directions. Employees are immediately and fully vested in their contributions. Our 401(k) Plan is intended to be qualified under Section 401(a) of the Code with our 401(k) Plan's related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to our 401(k) Plan and earnings on those contributions are not taxable to the employees until distributed from our 401(k) Plan.

Limitations on Liability and Indemnification

As permitted by Delaware law, provisions in our amended and restated certificate of incorporation and amended and restated bylaws limit or eliminate the personal liability of directors for a breach of their fiduciary duty of care as a director. The duty of care generally requires that, when acting on behalf of the corporation, a director exercise an informed business judgment based on all material information reasonably available to him or her. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any act related to unlawful stock repurchases, redemptions or other distributions or payments of dividends; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not limit or eliminate our rights or any stockholder's rights to seek non-monetary relief, such as injunctive relief or rescission. These provisions will not alter a director's liability under other laws, such as the federal securities laws or other state or federal laws. Our amended and restated certificate of incorporation also authorizes us to indemnify our officers, directors and other agents to the fullest extent permitted under Delaware law.

As permitted by Delaware law, our amended and restated bylaws provide that:

- we will indemnify our directors, officers, employees and other agents to the fullest extent permitted by law;
- we must advance expenses to our directors and officers, and may advance expenses to our employees and other agents, in connection with a legal proceeding to the fullest extent permitted by law; and
- the rights provided in our amended and restated bylaws are not exclusive.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director or officer, then the liability of our directors or officers will be so eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated bylaws will also permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in connection with their services to us, regardless of whether our bylaws permit such indemnification. We have obtained such insurance.

In addition to the indemnification that is provided for in our amended and restated certificate of incorporation and amended and restated bylaws, we have entered into indemnification agreements with each of our directors and executive officers, which may be broader than the specific indemnification provisions contained in the Delaware General Corporation Law. These indemnification agreements may require us, among other things, to indemnify our directors and executive officers for some expenses, including

attorneys' fees, expenses, judgments, fines and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of his service as one of our directors or executive officers or any other company or enterprise to which the person provides services at our request. We believe that these provisions and agreements are necessary to attract and retain qualified individuals to serve as directors and executive officers.

This description of the indemnification provisions of our amended and restated certificate of incorporation, our amended and restated bylaws and our indemnification agreements is qualified in its entirety by reference to these documents, each of which is attached as an exhibit to this Annual Report.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended (the Securities Act), may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable.

There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

Health and Welfare Benefits

All of our named executive officers are eligible to participate in our employee benefit plans, including our medical, dental and vision insurance plans, in each case on the same basis as all of our other full-time employees.

We believe the perquisites described above are necessary and appropriate to provide a competitive compensation package to our named executive officers.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. The director or officer may amend or terminate the plan in some circumstances. Our directors and executive officers may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Employment Arrangements and Severance Agreements with our Named Executive Officers

We have entered into employment agreements with each of our named executive officers.

Garry Menzel

In December 2018, we entered into an employment agreement with Dr. Menzel, effective upon the closing of the IPO, pursuant to which Dr. Menzel is entitled to receive an annual base salary of $500,000 and an annual target bonus equal to 50% of his annual base salary based upon our board of directors' or the compensation committee of the board of directors' assessment of Dr. Menzel's performance and our performance. This employment agreement also includes a reaffirmation of Dr. Menzel's Employee Confidentiality and Assignment Agreement, which contains continuing obligations to us, including provisions on proprietary information, assignment of inventions, non-competition and non-solicitation of customers and employees. Dr. Menzel's employment agreement provides that, in the event that his employment is terminated by us without "cause" or by him for "good reason," then subject to the execution and effectiveness of a separation agreement and release, he will be entitled to receive (i) an amount equal to (x) 12 months of base salary payable on our normal payroll cycle if such termination is not in connection with a "change in control" or (y) 18 months of base salary if such termination is in connection with a "change in control," payable on our normal payroll cycle, provided that in either case, if Dr. Menzel commences new employment, all payments shall cease; and (ii) payment of the monthly employer COBRA premium for the same level of group health coverage as in effect for Dr. Menzel on the date of termination up to (x) 12 months if such termination is not in connection with a "change in control," and (y) 18 months if such termination is in connection with a "change in control." In addition, if within 12 months following a "change in control," Dr. Menzel's employment is terminated by us without "cause" or he resigns for "good reason," then subject to the execution of the separation agreement and release, all time-based stock options and other time-based stock-based awards held by Dr. Menzel will accelerate and vest immediately.

Alfonso Quintás Cardama

In December 2018, we entered into an employment agreement with Dr. Quintás Cardama, effective upon the closing of the IPO, pursuant to which Dr. Quintás Cardama is entitled to receive an annual base salary of $430,000 and an annual target bonus equal to 35% of his annual base salary based upon our board of directors' or the compensation committee of the board of directors'

assessment of Dr. Quintás Cardama's performance and our performance. This employment agreement also includes a reaffirmation of Dr. Quintás Cardama's Employee Confidentiality and Assignment Agreement, which contains continuing obligations to us including provisions on proprietary information, assignment of inventions, non-competition and non-solicitation of customers and employees. Dr. Quintás Cardama's employment agreement provides that, in the event that his employment is terminated by us without "cause" or by him for "good reason," then subject to the execution and effectiveness of a separation agreement and release, he will be entitled to receive (i) an amount equal to (x) nine months of base salary payable on our normal payroll cycle if such termination is not in connection with a "change in control" or (y) 12 months of base salary if such termination is in connection with a "change in control," payable on our normal payroll cycle, provided that in either case, if Dr. Quintás Cardama commences new employment, all payments shall cease; and (ii) payment of the monthly employer COBRA premium for the same level of group health coverage as in effect for Dr. Quintás Cardama on the date of termination for up to (x) nine months if such termination is not in connection with a "change in control," and (y) 12 months if such termination is in connection with a "change in control." In addition, if within 12 months following a "change in control," Dr. Quintás Cardama's employment is terminated by us without "cause" or he resigns for "good reason," then subject to the execution of the separation agreement and release, all time-based stock options and other time-based stock-based awards held by Dr. Quintás Cardama will accelerate and vest immediately.

Ian (Mayur) Somaiya

In December 2018, we entered into an employment agreement with Mr. Somaiya, effective upon the closing of the IPO, pursuant to which Mr. Somaiya is entitled to receive an annual base salary of $375,000 and an annual target bonus equal to 35% of his annual base salary based upon our board of directors' or the compensation committee of the board of directors' assessment of Mr. Somaiya's performance and our performance. This employment agreement also includes a reaffirmation of Mr. Somaiya's Employee Confidentiality and Assignment Agreement, which contains continuing obligations to us including provisions on proprietary information, assignment of inventions, non-competition and non-solicitation of customers and employees. Mr. Somaiya's employment agreement provides that, in the event that his employment is terminated by us without "cause" or by him for "good reason," then subject to the execution and effectiveness of a separation agreement and release, he will be entitled to receive (i) an amount equal to (x) nine months of base salary payable on our normal payroll cycle if such termination is not in connection with a "change in control" or (y) 12 months of base salary if such termination is in connection with a "change in control," payable on our normal payroll cycle, provided that in either case, if Mr. Somaiya commences new employment, all payments shall cease; and (ii) payment of the monthly employer COBRA premium for the same level of group health coverage as in effect for Mr. Somaiya on the date of termination for up to (x) nine months if such termination is not in connection with a "change in control," and (y) 12 months if such termination is in connection with a "change in control." In addition, if within 12 months following a "change in control," Mr. Somaiya's employment is terminated by us without "cause" or he resigns for "good reason," then subject to the execution of the separation agreement and release, all time-based stock options and other time-based stock-based awards held by Mr. Somaiya will accelerate and vest immediately.

Outstanding Equity Awards

The following table sets forth information concerning outstanding equity awards held by our named executive officers as of December 31, 2020.

	Option Awards				
NAME	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS (#) EXERCISABLE	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS (#) UNEXERCISABLE		OPTION EXERCISE PRICE ($)	OPTION EXPIRATION DATE
Garry Menzel	169,054	-	(1)	$ 0.74	12/13/2026
	107,983	35,994	(2)	$ 0.74	12/7/2027
	261,630	171,407	(3)	$ 5.88	7/25/2028
	232,925	253,181	(4)	$ 16.11	4/10/29
	-	168,000	(5)	$ 16.10	12/18/2029
	-	245,000	(6)	$ 31.83	12/9/30
Alfonso Quintás Cardama	59,048	15,534	(7)	$ 0.74	10/9/2027
	31,762	10,584	(2)	$ 0.74	12/7/2027
	54,809	35,910	(3)	$ 5.88	7/25/2028
	101,248	110,054	(4)	$ 16.11	4/10/2029
	-	72,100	(5)	$ 16.10	12/18/2029
	-	101,000	(6)	$ 31.83	12/9/30
Mayur (Ian) Somaiya	67,039	35,519	(8)	$ 5.88	4/29/2028
	17,167	11,248	(3)	$ 5.88	7/25/2028
	72,980	79,327	(4)	$ 16.11	4/10/2029
	-	50,000	(5)	$ 16.10	12/18/2029
	-	92,000	(6)	$ 31.83	12/9/30

Option awards vest over four years, with 25% vesting on the first anniversary of the vesting commencement date, and the remainder vesting in 36 equal monthly installments thereafter, subject to continued employment with us.

(1) Represents stock option granted on December 13, 2016.

(2) Represents stock option granted on December 7, 2017.
(3) Represents stock option granted on July 26, 2018.
(4) Represents stock option granted on April 11, 2019.
(5) Represents stock option granted on December 19, 2019.
(6) Represents stock option granted on December 10, 2020.
(7) Represents stock option granted on October 10, 2017.
(8) Represents stock option granted on April 30, 2018.

Compensation Risk Assessment

We believe that although a portion of the compensation provided to our executive officers and other employees is performance-based, our executive compensation program does not encourage excessive or unnecessary risk taking.

This is primarily due to the fact that our compensation programs are designed to encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on us.

Director Compensation

The following table presents the total compensation for each person who served as a non-employee member of our board of directors and received compensation for such service during the year ended December 31, 2020. Other than as set forth in the table and described more fully below, we did not pay any compensation, make any equity awards to, or pay any other compensation to any of the non-employee members of our board of directors in 2020. Dr. Menzel, our President and Chief Executive Officer, did not receive any compensation for his service as a member of our board of directors. Dr. Menzel's compensation for service as an employee for year ended December 31, 2020 is presented in "Executive Compensation—Summary Compensation Table." We reimburse members of our board of directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of directors and committee meetings.

Director Compensation Table — 2020

NAME	FEES EARNED OR PAID IN CASH ($)	OPTION AWARDS ($)(2)	ALL OTHER COMPENSATION ($)(3)	TOTAL ($)
Ansbert Gadicke (1)	$ -	$ -	$ -	$ -
Andrew Allen	51,250	252,164	-	303,414
Patrick Baeuerle (3)	-	252,164	51,988	304,152
Mitchell Finer (3)	-	-	18,750	18,750
Neil W. Gibson	56,250	252,164	-	308,414
Axel Hoos	27,448	315,402	-	342,850
Shawn Tomasello	-	-	-	-
Stephen Webster	33,333	315,370	-	348,703

(1) Investor-appointed directors did not receive fees, as directors, or other equity compensation for their service on our board of directors.

(2) Represents stock options granted in 2020. In accordance with SEC rules, these columns reflect the aggregate grant date fair value of the option awards granted during 2020 computed in accordance with Financial Accounting Standard Board ASC Topic 718 for stock-based compensation transactions.
(3) Drs. Baeuerle and Finer provided services to us pursuant to the terms of the consulting agreements with Dr. Baeuerle and Dr. Finer and Pattern Recognition Ventures, respectively. The cash fees presented above are related to these services for the year ended December 31, 2020. The amount for Dr. Finer include fees paid prior to his resignation from the board of directors.

Non-Employee Director Compensation Policy

Our board of directors has adopted a non-employee director compensation policy that is designed to enable us to attract and retain, on a long-term basis, highly qualified non-employee directors. Under the policy, each independent director who is not an employee or affiliated with one of our 5% holders is paid cash compensation for service on our board of directors and for service on each committee on which the director is a member. The chair of each committee receives a higher retainer for such service. These fees are payable in arrears in four equal quarterly instalments pro-rated based on the number of actual days served by the director during such calendar quarter. The fees paid to independent non-employee directors for service on our board of directors and for service on each committee of our board of directors on which the director is a member are set forth below:

	MEMBER ANNUAL FEE ($)	CHAIRMAN ADDITIONAL ANNUAL FEE ($)
Board of Directors	$ 35,000	$ 30,000
Audit Committee	7,500	15,000
Compensation Committee	5,000	10,000
Nominating and Corporate Governance Committee	4,000	8,000
Finance and Strategy Committee	—	—

In addition, each non-employee director elected or appointed to our board of directors that is not affiliated with a 5% holder of our stock will be granted an initial one-time equity award of a stock option with a grant date fair value of approximately $400,000, based on the current fair market value of the Company's common stock, which shall vest 25% on the one-year anniversary of the date of grant, with the remainder vesting in 24 equal monthly instalments, subject to continued service through such vesting date(s). In addition, at the end of each year, each non-employee director that is not affiliated with a 5% holder will be granted an equity award of stock options with a grant date fair market value of approximately $200,0000, based on the then fair market value of the Company's common stock, which will vest 25% on the one-year anniversary of the date of grant, with the remainder vesting in 36 equal monthly installments subject to continued service as a director through such vesting date(s).

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

Securities authorized for issuance under equity compensation plans

The following table provides information relating to our equity compensation plans as of December 31, 2020. As of December 31, 2020, we had two equity compensation plan, our 2018 Plan and our Employee Stock Purchase Plan, which were approved by our Board of Directors and our stockholders.

	Equity Compensation Plans		
	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted-average exercise price of outstanding options, warrants, and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
	(a)	(b)	(c)
Equity compensation plans approved by stockholders	5,223,042	$ 14.43	975,816
Equity compensation plans not approved by stockholders	—		—
Total	5,223,042		975,816

Security Ownership of Certain Beneficial Owners

The following table sets forth certain information known to us regarding beneficial ownership of our capital stock outstanding as of March 1, 2021 for:

- each person, or group of affiliated persons, who is known by us to be the beneficial owner of five percent or more of our outstanding common stock;
- each of our directors;
- each of our named executive officers; and
- all of our current directors and executive officers as a group.

We have determined beneficial ownership in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities as well as any shares of common stock that the person has the right to acquire within 60 days of March 1, 2021 through the exercise of stock options or other rights. These shares are deemed to be outstanding and beneficially owned by the person holding those options for the purpose of computing the

percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them. Each individual or entity shown on the table has furnished information with respect to beneficial ownership. Except as otherwise indicated below, the address of each officer, director and five percent stockholder listed below is c/o TCR2 Therapeutics Inc., 100 Binney Street, Suite 710, Cambridge, MA 02142.

The percentage of beneficial ownership in the table below is based on 38,137,440 shares of common stock deemed to be outstanding as of March 1, 2021.

	COMMON STOCK BENEFICIALLY OWNED	
	SHARES	PERCENTAGE
5% or Greater Stockholders		
Entities affiliated with MPM Capital (1)	4,229,134	11.04%
UBS Oncology Impact Fund, L.P. (2)	3,370,982	8.84%
Entites affiliated with Wellington Management Group LLP (3)	3,753,364	9.84%
Entities affiliated with Redmile Group, LLC (4)	2,832,888	7.43%
BlackRock, Inc. (5)	2,603,539	6.83%
Directors, Named Executive Officers and Other Executive Officers		
Garry Menzel (6)	963,629	2.47%
Mayur (Ian) Somaiya (7)	188,385	*
Alfonso Quintás Cardama (8)	293,506	*
Ansbert Gadicke (9)	7,600,116	19.84%
Andrew Allen (10)	9,230	*
Patrick Baeuerle (11)	436,656	1.14%
Neil Gibson (12)	9,230	*
Axel Hoos	—	*
Shawn Tomasello	—	*
Stephen Webster	—	*
All executive officers and directors as a group (12 persons) (13)	9,783,497	24.45%

* Less than one percent.

(1) Based solely on a Schedule 13D filed by MPM Asset Management on March 4, 2019, consists of (i) 110,859 shares of common stock held by MPM Asset Management Investors BV2014 LLC, (ii) 62,916 shares of common stock held by MPM Asset Management Investors SunStates Fund LLC, (iii) 195,902 shares of common stock and warrants to purchase 178,269 shares of common stock exercisable within 60 days of March 1, 2021, in each case held by MPM Asset Management LLC, (iv) 203,846 shares of common stock held by MPM BioVentures 2014 (B), L.P., (v) 3,056,272 shares of common stock held by MPM BioVentures 2014, L.P., and (vi) 421,070 shares of common stock held by MPM SunStates Fund, L.P. MPM BioVentures 2014 GP LLC is the general partner of MPM BioVentures 2014, L.P. and MPM BioVentures 2014 (B), L.P. MPM BioVentures 2014 LLC is the managing member of MPM BioVentures 2014 GP LLC and the manager of MPM Asset Management Investors BV2014 LLC. MPM SunStates Fund GP LLC is the general partner of MPM SunStates Fund, L.P. MPM SunStates GP Managing Member LLC is the managing member of MPM SunStates Fund GP LLC and the manager of MPM Asset Management Investors SunStates Fund LLC. MPM Asset Management LLC was retained as a manager to manage the operations of MPM BioVentures 2014, L.P., MPM BioVentures 2014 (B), L.P., MPM Asset Management Investors BV2014 LLC, MPM SunStates Fund, L.P., and MPM Asset Management SunStates Fund LLC. Dr. Ansbert Gadicke is a member of MPM BioVentures 2014 LLC, MPM SunStates GP Managing Member LLC, and MPM Capital, formerly known as MPM Asset Management LLC, and collectively with the other members of such entities makes investment decisions with respect to shares held by such entities. Each of the entities and individuals listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address of these entities and individuals is 450 Kendall Street, Cambridge, MA 02142.

(2) Based solely on a Schedule 13D filed by MPM Asset Management on March 4, 2019, consists of 3,370,982 shares of common stock held by UBS Oncology Impact Fund, L.P. The general partner of UBS Oncology Impact Fund, L.P. is Oncology Impact Fund (Cayman) Management L.P. The general partner of Oncology Impact Fund (Cayman) Management L.P. is MPM Oncology Impact Management LP. The general partner of MPM Oncology Impact Management LP is MPM Oncology Impact Management GP LLC. Dr. Ansbert Gadicke is a managing member and the managing director of MPM Oncology Impact Management GP LLC. Each of the entities and individuals listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address of these entities and individuals is Durell House, 28 New Street, St Helier, Jersey, JE1 4FS.

(3) Based solely on a Schedule 13G filed by Wellington Management Group LLP on January 11, 2021, consists of 3,753,364 shares of common stock held Wellington Management Group LLP and related entities. The address of this entity is 280 Congress Street, Boston, MA 02210.

(4) Based solely on a Schedule 13G/A filed by Redmile Group, LLC on February 16, 2021, consists of 2,832,888shares of common stock owned by certain private investment vehicles and/or separately managed accounts managed by Redmile Group, LLC, which shares of common Stock may be deemed beneficially owned by Redmile Group, LLC as investment manager of such private investment vehicles and/or separately managed accounts. The reported securities may also be deemed beneficially owned by Jeremy C. Green as the principal of Redmile Group, LLC. Redmile Group, LLC and Mr. Green each disclaim beneficial ownership of these shares, except to the extent of its or his pecuniary interest in such shares, if any. The address of these entities and individuals is One Letterman Drive, Building D, Suite D3-300, The Presidio of San Francisco, San Francisco, California 94129

(5) Based solely on a Schedule 13G filed by BlackRock, Inc. on February 2, 2021, consists of 2,603,539 shares of common stock held by BlackRock, Inc. The address of this entity is 55 East 52nd Street, New York, NY 10055.

(6) Consists of (i) 4,085 shares of common stock, (ii) options to purchase 875,017 shares of common stock exercisable within 60 days of March 1, 2021 and (ii) 84,527 shares of common stock held by Dr. Garry Menzel, as Trustee of the Garry E. Menzel and Mary E. Henshall Family Trust, under instrument of trust dated July 29, 2010. Dr. Menzel is the trustee of the Garry E. Menzel and Mary E. Henshall Family Trust and may be deemed to beneficially own these securities.

(7) Consists of (i) 1,473 shares of common stock and (ii) options to purchase 186,912 shares of common stock exercisable within 60 days of March 1, 2021.

(8) Consists of (i) 3,751 shares of common stock and (ii) options to purchase 289,755 shares of common stock exercisable within 60 days of March 1, 2021.

(9) See notes (1) and (3) above.

(10) Consists of options to purchase 9,230 shares of common stock exercisable within 60 days of March 1, 2021.

(11) Consists of options to purchase 85,870 shares of common stock exercisable within 60 days of March 1, 2021 and (ii) 350,786 shares of common stock held by APAK Solutions GmbH. Dr. Baeuerle is a managing director of APAK Solutions GmbH and shares voting and investment power with respect to these shares. Each of the entities and individuals listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address of these entities and individuals is c/o MPM Capital, 450 Kendall Street, Cambridge, MA 02142.

(12) Consists of (i) options to purchase 9,230 shares of common stock held by Dr. Neil Gibson exercisable within 60 days of March 1, 2021.

(13) Consists of (i) 7,914,645 shares common stock, (ii) options to purchase 1,690,583 shares of common stock exercisable within 60 days of March 1, 2021 and (iii) warrants to purchase 178,269 shares of common stock exercisable within 60 days of March 21, 2020, held by ten executive officers and directors, and entities affiliated with such executive officers and directors, as described in notes (6) through (12) above.

Communications with the Board of Directors

Stockholders who want to communicate with members of the Board, including the independent directors, individually or as a group, should address their communications to the Board, the Board members or the Board committee, as the case may be, and send them by mail to c/o TCR2 Therapeutics Inc., 100 Binney Street, Suite 710, Cambridge, Massachusetts 02142. The Chair of the Audit Committee will forward all such communications directly to such Board members. Any such communications may be made on an anonymous and confidential basis.

A copy of any such written communication may also be forwarded to the Company's legal counsel and a copy of such communication may be retained for a reasonable period of time. The director may discuss the matter with the Company's legal counsel, with independent advisors, with non-management directors, or with the Company's management, or may take other action or no action as the director determines in good faith, using reasonable judgment, and applying his or her own discretion.

The Audit Committee oversees the procedures for the receipt, retention, and treatment of complaints received by the Company regarding accounting, internal accounting controls, or audit matters, and the confidential, anonymous submission by employees of concerns regarding questionable accounting, internal accounting controls or auditing matters. The Company has also established a toll-free telephone number for the reporting of such activity, which is 877-865-0978.

Board Committees

Our Board of Directors has established an Audit Committee, a Compensation Committee and a Nominating and Corporate Governance committee, each of which operates pursuant to a charter adopted by our Board of Directors. Our Board of Directors has also established a Finance and Strategy committee. We believe that the composition and functioning of all of our committees will comply with the applicable requirements of Nasdaq, the Sarbanes-Oxley Act of 2002 and SEC rules and regulations that will be applicable to us. We intend to comply with future requirements to the extent they become applicable to us.

The full text of our Audit Committee charter, Compensation Committee charter, and Nominating and Corporate Governance charter are posted on the investor relations portion of our website at www.tcr2.com. We do not incorporate the information contained on, or accessible through, our corporate website into this Annual Report, and you should not consider it a part of this Annual Report.

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

The following is a description of transactions or series of transactions since January 1, 2019 to which we were or will be a party, in which:

- the amount involved in the transaction exceeds, or will exceed, $120,000 (or, if less, 1% of the average of our total assets amounts at December 31, 2019 and 2020); and
- in which any of our executive officers, directors or holder of five percent or more of any class of our capital stock, including their immediate family members or affiliated entities, had or will have a direct or indirect material interest.

Compensation arrangements for our named executive officers and our directors are described elsewhere in this Annual Report under "Director Compensation" and "Executive Compensation."

All amounts in thousands unless otherwise noted

Manufacturing agreement

During November 2020, we entered into a manufacturing partnership with ElevateBio, LLC. Dr. Ansbert Gadicke is a member of the board of directors at the Company and ElevateBio, LLC. The agreement is to establish a manufacturing partnership with ElevateBio, LLC for production of the Company's clinical trial products. During the year ended December 31, 2020, we incurred $760 in expenses and have incurred additional costs of $1,600 for equipment owned by us for use by ElevateBio, LLC.

Participation in our Initial Public Offering

Certain of our directors, executive officers and our 5% stockholders purchased shares of our common stock in our IPO at the initial public offering price. The following table sets forth the number of shares of our common stock purchased by directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares.

	Shares of Common Stock Purchased		Aggregate Cash Purchase Price
Entities affiliated with MPM Capital	1,373,333	$	20,599,995
Entities affiliated with Redmile Group	1,000,000	$	15,000,000
UBS Oncology Impact Fund L.P.	666,667	$	10,000,005

Harpoon Therapeutics, Inc. License Agreement

In June 2017, we entered into a license agreement with Harpoon Therapeutics, Inc. (Harpoon), under which Harpoon provides us with rights to use certain Harpoon intellectual property relating to antibody-based protein binders and related know-how developed by Harpoon. In return, we provide Harpoon with the right to use antibody-based protein binders developed by us. Each license granted under this Harpoon license agreement is non-exclusive. Affiliates of MPM Capital that own shares of our common stock are founding stockholders in Harpoon, and Dr. Patrick Baeuerle, one of our directors and co-founders, is a director and co-founder of Harpoon.

Amended and Restated Investors' Rights Agreement

We are a party to an amended and restated investors' rights agreement, or the Investors' Rights Agreement, dated as of February 28, 2018, with holders of our previously-outstanding Series A preferred stock and Series B preferred stock, including certain of our 5% stockholders and their affiliates and entities affiliated with certain of our officers and directors. The Investors' Rights Agreement provides these holders the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing.

Employment Agreements

We have entered into employment agreements with certain of our executive officers. See "Item 11-Executive Compensation—Employment Arrangements and Severance Agreements with our Named Executive Officers"

Equity Grants

We have granted stock options and warrants to certain of our executive officers and members of our board of directors. See "Item 11-Executive Compensation"

Indemnification Agreements

As permitted by Delaware law, provisions in our amended and restated certificate of incorporation and amended and restated bylaws limit or eliminate the personal liability of directors for a breach of their fiduciary duty of care as a director. In addition, we have entered into indemnification agreements with each of our executive officers and the members of our board of directors which may require us to indemnify them. See "Item 11-Executive Compensation—Limitations on Liability and Indemnification"

Policies for Approval of Related Party Transactions

Our board of directors reviews and approves transactions with directors, officers and holders of 5% or more of our voting securities and their affiliates, each a related party. Prior to our initial public offering, the material facts as to the related party's relationship or interest in the transaction were disclosed to our board of directors prior to their consideration of such transaction, and the transaction was not considered approved by our board of directors unless a majority of the directors who are not interested in the transaction approved the transaction. Further, when stockholders were entitled to vote on a transaction with a related party, the material facts of the related party's relationship or interest in the transaction were disclosed to the stockholders, who must have approved the transaction in good faith.

In connection with our initial public offering, our board of directors adopted a written related party transactions policy. Pursuant to this policy, the audit committee has the primary responsibility for reviewing and approving or disapproving "related party transactions," which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed $120,000 and in which a related person has or will have a direct or indirect material interest. For purposes of this policy, a related person will be defined as a director, executive officer, nominee for director, or greater than 5% beneficial owner of our common stock, in each case since the beginning of the most recently completed year, and their immediate family members.

Director Independence

Under the Nasdaq listing rules, independent directors must comprise a majority of a listed company's board of directors within twelve months from the date of listing. In addition, the Nasdaq listing rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and governance committees be independent within twelve months from the date of listing. Audit committee members must also satisfy additional independence criteria, including those set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended (the Exchange Act), and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under Nasdaq listing rules, a director will only qualify as an "independent director" if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3 under the Exchange Act, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors or any other board committee: (1) accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries, other than compensation for board service; or (2) be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board of directors must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director, and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In March 2021, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that all members of our board of directors, except Garry Menzel, are independent directors, including for purposes of Nasdaq and SEC rules. In making that determination, our board of directors considered the relationships that each director has with us and all other facts and circumstances the board of directors deemed relevant in determining independence, including the potential deemed beneficial ownership of our capital stock by each director, including non-employee directors that are affiliated with certain of our major stockholders. There are no family relationships among any of our directors or executive officers.

Audit Committee

As of March 1, 2021, our audit committee consists of Andrew Allen, Neil Gibson and Stephen Webster and is chaired by Stephen Webster. The functions of the audit committee include:

- appointing, approving the compensation of and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our consolidated financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly consolidated financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee's review and discussions with management and our independent registered public accounting firm whether our audited consolidated financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our consolidated financial statements and our compliance with legal and regulatory requirements as they relate to our consolidated financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related party transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases.

All members of our audit committee will meet the requirements for financial literacy under the applicable rules and regulations of the SEC and the Nasdaq listing rules. Our board of directors has determined that Andrew Allen, Neil Gibson and Stephen Webster are "independent" for audit committee purposes as that term is defined in the rules of the SEC and the current listing standards of Nasdaq. Our board of directors has determined that Stephen Webster is an audit committee financial expert.

The audit committee held four meetings during 2020. The audit committee operates under a written charter that satisfies the applicable standards of the SEC and Nasdaq. A copy of the audit committee charter is available on our website at investors.tcr2.com/corporate-governance/governance-overview. We do not incorporate the information contained on, or accessible through, our corporate website into this Annual Report, and you should not consider it a part of this Annual Report.

Compensation Committee

As of March 1, 2021, our compensation committee consists of Andrew Allen, Shawn Tomasello and Neil Gibson, and is chaired by Neil Gibson. The functions of the compensation committee include:

- annually reviewing and recommending to the board of directors the corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and based on such evaluation (i) reviewing and determining the cash compensation of our Chief Executive Officer and (ii) reviewing and approving grants and awards to our Chief Executive Officer under our equity-based plans;
- reviewing and approving the compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- evaluating and assessing potential and current compensation advisors in accordance with the independence standards identified in the applicable Nasdaq listing rules;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and recommending to the board of directors the compensation of our directors;
- preparing our compensation committee report if and when required by SEC rules;
- reviewing and discussing annually with management our “Compensation Discussion and Analysis,” if and when required, to be included in our annual proxy statement; and
- reviewing and approving the retention or termination of any consulting firm or outside adviser to assist in the evaluation of compensation matters.
-

Each member of our compensation committee is a non-employee director, as defined in Rule 16b-3 promulgated under the Exchange Act, and an outside director, as defined pursuant to Section 162(m) of the Internal Revenue Code of 1986, as amended (the Code).

The compensation committee held one meeting during 2020. The compensation committee operates under a written charter that satisfies the applicable standards of the SEC and Nasdaq. A copy of the compensation committee charter is available on our website at investors.tcr2.com/corporate-governance/governance-overview. We do not incorporate the information contained on, or accessible through, our corporate website into this Annual Report, and you should not consider it a part of this Annual Report.

Nominating and Corporate Governance Committee

As of March 1, 2021, our nominating and corporate governance committee consists of Ansbert Gadicke, Axel Hoos Shawn Tomasello and is chaired by Ansbert Gadicke. The functions of the nominating and corporate governance committee include:

- developing and recommending to the board of directors’ criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- reviewing the composition of the board of directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board’s committees;
- developing and recommending to the board of directors a code of business conduct and ethics and a set of corporate governance guidelines; and
- overseeing the evaluation of our board of directors and management.

The nominating and corporate committee held three meetings during 2019. The nominating and corporate committee operates under a written charter that satisfies the applicable standards of the SEC and Nasdaq. A copy of the nominating and corporate committee charter is available on our website at investors.tcr2.com/corporate-governance/governance-overview. We do not incorporate the information contained on, or accessible through, our corporate website into this Annual Report, and you should not consider it a part of this Annual Report.

Finance and Strategy Committee

Our finance and strategy committee consists of Ansbert Gadicke, Andrew Allen and Stephen Webster and is chaired by Ansbert Gadicke. The purpose of the finance and strategy committee is to consider and make recommendations to our board of directors regarding issues impacting our financial structure and strategic direction, including, but not limited to, our capital structure, business development activities and financing strategy, as well as the overall scope and focus of our business and operations. The finance and strategy committee held one meeting during 2019.

Our board of directors may from time to time establish other committees.

Director Affiliations

Some of our directors are affiliated with and serve on the board of directors as representatives of entities which beneficially own or owned 5% or more of our common stock, as indicated below:

Name	Principal Stockholder
Ansbert Gadicke	MPM Capital and UBS Oncology Impact Fund, L.P.

Item 14. Principal Accountant Fees and Services

The Audit Committee has selected KPMG LLP as our independent registered public accounting firm for the years ended December 31, 2020 and 2019. In addition to retaining KPMG LLP to audit our consolidated financial statements for years ended December 31, 2020 and 2019, we may engage the firm from time to time during the year to perform other services.

The following table sets forth the aggregate fees billed by KPMG LLP in connection with services rendered during the last two fiscal years.

	For the Year Ended	
	2020	2019
Audit fees	$ 598,000	$ 403,000
Audit-related fees	—	—
Tax fees	—	20,000
Other fees	1,780	1,780
	$ 599,780	$ 424,780

Audit Fees consist of fees for professional services rendered in connection with the audit of our annual consolidated financial statements, the review of the interim consolidated financial statements included in quarterly reports, services rendered in connection with SEC registration statements, and services that are normally provided by KPMG LLP, such as comfort letters, in connection with statutory and regulatory filings or engagements.

Tax Fees consist of fees for professional services rendered for tax compliance and tax advice.

All Other Fees consist of accounting research software license fees.

In fiscal 2020 and 2019, no services other than those discussed above were provided by KPMG LLP.

The Audit Committee has adopted a policy requiring pre-approval of all audit and non-audit related services to be performed by the Company's independent auditor regardless of amount. These services may include audit services, audit-related services, tax services and other related services. KPMG LLP and management are required to periodically report to the Audit Committee regarding the extent of services provided by KPMG LLP in accordance with this pre-approval and the fees for the services performed to date. The Audit Committee may also pre-approve particular services on a case-by-case basis.

The Audit Committee annually evaluates the qualifications, performance and independence of the Company's independent registered public accounting firm. It selected KPMG as the Company's independent registered public accounting firm for 2019. This selection was subsequently approved by the Board. The Audit Committee has reviewed and discussed with management and with KPMG the Company's audited consolidated financial statements for the year ended December 31, 2020. In addition, the Audit Committee has discussed with KPMG the matters that independent registered public accounting firms must communicate to audit committees under applicable PCAOB standards.

The Audit Committee has also discussed and confirmed with KPMG its independence from the Company and received all written disclosures and correspondence required by the PCAOB Ethics and Independence requirement s. The Audit Committee has evaluated and concluded the non-audit services provided by KPMG to the Company do not impair KPMG's independence.

Based on the reviews and discussions referred to above, the Audit Committee recommended to our Board that the audited consolidated financial statements for the year ended December 31, 2020 and the related footnotes be included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

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

Not applicable.

EXHIBIT INDEX

Number	EXHIBIT DESCRIPTION	FORM	FILE NO.	EXHIBIT	FILING DATE	FILED HEREWITH
3.1	Amended and Restated Certificate of Incorporation of the Registrant	8-K	001-38811	3.1	2/25/2019	
3.2	Amended and Restated By-laws of the Registrant	8-K	001-38811	3.2	2/25/2019	
3.3	Amendment No. 1 to Amended and Restated By-Laws of the Registrant					X
4.1	Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, dated February 28, 2018	S-1	333-229066	4.1	12/28/2018	
4.2	Form of Specimen Common Stock Certificate	S-1	333-229066	4.2	2/1/2019	
4.3	Form of Common Stock Warrant	S-1	333-229066	4.3	12/28/2018	
4.4	Description of Registrant's Securities					X
10.1#	2015 Stock Option and Grant Plan and forms of award agreements thereunder	S-1	333-229066	10.1	12/28/2018	
10.2#	2018 Stock Option and Incentive Plan and forms of award agreements thereunder	S-1	333-229066	10.2	2/1/2019	
10.3#	Senior Executive Cash Incentive Bonus Plan	S-1	333-229066	10.3	12/28/2018	
10.4#	2018 Employee Stock Purchase Plan	S-1	333-229066	10.4	2/1/2019	
10.5#	Form of Director Indemnification Agreement	S-1	333-229066	10.5	12/28/2018	
10.6#	Form of Officer Indemnification Agreement	S-1	333-229066	10.6	12/28/2018	
10.7	Lease Agreement, dated as of June 30, 2017, by and between ARE-MA Region No. 45, LLC and the Registrant	S-1	333-229066	10.7	12/28/2018	
10.8#	Form of Amended and Restated Employment Agreement	S-1	333-229066	10.8	12/28/2018	
10.9†	License Agreement, dated as of June 21, 2017, by and between Harpoon Therapeutics, Inc. and the Registrant	S-1	333-229066	10.9	12/28/2018	
10.10	Royalty Transfer Agreement, dated as of May 26, 2016, by and among the Registrant, MPM Oncology Charitable Foundation, Inc. and the UBS Optimus Foundation	S-1	333-229066	10.13	12/28/2018	
10.11	Letter Agreement, dated as of May 26, 2016, by and among the Registrant, MPM Oncology Charitable Foundation, the UBS Optimus Foundation and UBS Oncology Impact Fund L.P.	S-1	333-229066	10.14	12/28/2018	
10.12†	Collaboration Agreement, dated as of December 18, 2018, by and between the Registrant and Cell Therapy Catapult Limited	S-1	333-229066	10.15	12/28/2018	
10.13#	Amendment #1 to 2018 Stock Option and Incentive Plan	10-Q	001-38811	10.1	5/13/2019	
21.1	Subsidiaries of the Registrant	S-1	333-229066	21.1	2/1/2019	
23.1	Consent of KPMG LLP, Independent Registered Public Accounting Firm					X
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) / Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended					X
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) / Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended					X
32.1+	Certifications of the Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
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					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X
EX-104	Cover Page Interactive Data File (embedded within the Inline XBRL document)					
#	Indicates a management contract or any compensatory plan, contract or arrangement					
†	Confidential treatment has been granted as to certain portions of this exhibit, which portions have been omitted and submitted separately to the Securities and Exchange Commission.					

+ The certifications furnished in Exhibit 32.1 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 the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

TCR2 THERAPEUTICS INC.

March 16, 2021

By: /s/ Garry E. Menzel
Garry E. Menzel
President, Chief Executive Officer and Director
(Principal Executive Officer)

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Garry E. Menzel and Mayur (Ian) Somaiya, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Garry E. Menzel Garry E. Menzel	President, Chief Executive Officer and Director (Principal Executive Officer)	March 16, 2021
/s/ Mayur (Ian) Somaiya Mayur (Ian) Somaiya	Chief Financial Officer (Principal Financial and Accounting Officer)	March 16, 2021
/s/ Ansbert Gadicke Ansbert Gadicke	Director	March 16, 2021
/s/ Andrew Allen Andrew Allen	Director	March 16, 2021
/s/ Patrick Baeuerle Patrick Baeuerle	Director	March 16, 2021
/s/ Neil Gibson Neil Gibson	Director	March 16, 2021
/s/ Alex Hoos Alex Hoos	Director	March 16, 2021
/s/ Shawn Tomasello Shawn Tomasello	Director	March 16, 2021
/s/ Stephen Webster Stephen Webster	Director	March 16, 2021

Exhibit 3.3

AMENDMENT NO. 1 TO THE AMENDED AND RESTATED BY-LAWS
OF
TCR2 THERAPEUTICS INC.
(THE "COMPANY")

Section 8 of Article VI of the Amended and Restated By-laws of the Company (the "By-laws"), is hereby amended and restated in its entirety to read as follows:

"SECTION 8. Exclusive Jurisdiction of Delaware Courts or the United States Federal District Courts. Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on behalf of the Corporation, (ii) any action asserting a claim of, or a claim based on, a breach of a fiduciary duty owed by any current or former director, officer or other employee of the Corporation to the Corporation or the Corporation's stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law or the Certificate or Bylaws (including the interpretation, validity or enforceability thereof), or (iv) any action asserting a claim governed by the internal affairs doctrine. Unless the Corporation consents in writing to the selection of an alternative forum, the federal district courts of the United States of America shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. Any person or entity purchasing or otherwise acquiring any interest in shares of capital stock of the Corporation shall be deemed to have notice of and consented to the provisions of this Section 8."

The remainder of the By-laws remain in full force and effect.

Adopted and effective as of March 15, 2021.

Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934, as amended

The common stock, par value $0.0001 per share ("Common Stock"), of TCR2 Therapeutics Inc. ("TCR2," "we," or "our") is registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The following description sets forth certain general terms and provisions of our Common Stock. These descriptions are in all respects subject to and qualified in their entirety by, and should be read in conjunction with, the applicable provisions of our Amended and Restated Certificate of Incorporation (our "Charter") and our Amended and Restated By-laws (our "By-laws"), each of which is incorporated herein by reference and copies of which are incorporated by reference as exhibits to our most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission, and the applicable provisions of General Corporation Law of the State of Delaware (the "DGCL").

Authorized Capital Stock

We are authorized to issue 150,000,000 shares of Common Stock and 10,000,000 shares of preferred stock, par value $0.0001 per share ("Preferred Stock").

Common Stock

The holders of Common Stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of Common Stock do not have any cumulative voting rights. Holders of Common Stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. The Common Stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of Common Stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding Preferred Stock.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of Preferred Stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of Common Stock. The issuance of our Preferred Stock could adversely affect the voting power of holders of Common Stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of Preferred Stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action.

Registration Rights

Pursuant to the terms of our Amended and Restated Investors' Rights Agreement, dated as of February 28, 2018, with certain of our stockholders (the "Investors' Rights Agreement"), certain of our stockholders are entitled to rights with respect to the registration of their shares (which we refer to herein as "registrable securities") under the Securities Act of 1933, as amended (the "Securities Act"), including demand registration rights, short-form registration rights and piggyback registration rights.

Demand Registration Rights

The holders of our registrable securities are entitled to demand registration rights. Under the terms of the Investors' Rights Agreement, we will be required, upon the written request of holders of at least a majority of our outstanding registrable securities, to file a registration statement with respect to at least 40% of the securities eligible for registration then outstanding (or a lesser percent if the anticipated aggregate offering price, net of related fees and expenses, would exceed $5 million). We are required to effect up to two registrations pursuant to this provision of the Investors' Rights Agreement.

Short-Form Registration Rights

The holders of our registrable securities are entitled to short-form registration rights. Pursuant to the Investors' Rights Agreement, upon the written request of stockholders holding at least 10% of the outstanding registrable securities having an anticipated aggregate offering, net of related fees and expenses, of at least $1.0 million, we will be required to file a Form S-3 registration restatement covering all outstanding registrable securities that our stockholders request to be included in such registration. We are required to effect only two registrations in any twelve-month period pursuant to this provision of the Investors' Rights Agreement. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Piggyback Registration Rights

Pursuant to the Investors' Rights Agreement, if we register any of our securities either for our own account or for the account of other security holders, the holders of our outstanding registrable securities are entitled to include their shares in the registration. Subject to certain exceptions contained in the Investors' Rights Agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

The Investors' Rights Agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The registration rights granted under the Investors' Rights Agreement will terminate the earliest to occur of: (i) on the fifth anniversary of the our initial public offering, (ii) at such time after our initial public offering when all registrable securities could be sold under Rule 144 of the Securities Act or another similar exemption without restriction within a three-month period or (iii) a merger, sale or liquidation of our company.

Anti-Takeover Effects of Delaware Law and Certain Provisions of our Charter and Bylaws

Our Charter and Bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

Our Charter provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our Charter also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

Our Charter provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our Bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of Stockholders

Our Charter and Bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our Bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our Bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our Bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to Charter and Bylaws

Any amendment of our Charter must first be approved by a majority of our board of directors, and if required by law or our Charter, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our Bylaws and Charter must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than a majority of the outstanding shares of each class entitled to vote thereon as a class. Our Bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the Bylaws; and may also be amended by the affirmative vote of at least two-thirds of the outstanding shares entitled to vote on the amendment, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated Preferred Stock

Our Charter provides for 10,000,000 authorized shares of Preferred Stock. The existence of authorized but unissued shares of Preferred Stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of Preferred Stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our Charter grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of Preferred Stock. The issuance of shares of Preferred Stock could decrease the amount of earnings and assets available for distribution to holders of shares of Common Stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the DGCL. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Choice of Forum

Our Bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claim for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws (including the interpretation, validity or enforceability thereof) or (iv) any action asserting a claim that is 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 or the Exchange Act. In addition, our amended and restated bylaws will further provide that unless we consent in writing to the selection of an alternate forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the "Federal Forum Provision"). 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 Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with U.S. federal securities laws and the rules and regulations thereunder.

We recognize that the Delaware Forum Provision and the Federal Forum Provision in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims. 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. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the United States 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.

Stock Exchange Listing

Our Common Stock is listed on The Nasdaq Global Select Market under the trading symbol "TCRR."

Transfer Agent and Registrar

The Transfer Agent and Registrar for our Common Stock is the American Stock Transfer & Trust Company, LLC.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
TCR2 Therapeutics Inc.:

We consent to the incorporation by reference in the registration statements (Nos. 333-236965 and 333-252244) on Form S-3 and (Nos. 333-229691 and 333-237481) on Form S-8 of TCR2 Therapeutics Inc. of our report dated March 16, 2021, with respect to the consolidated balance sheets of TCR2 Therapeutics Inc. and subsidiaries as of December 31, 2020 and 2019, the related consolidated statements of operations, comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for the years then ended, and the related notes, which report appears in the December 31, 2020 annual report on Form 10-K of TCR2 Therapeutics Inc.

/s/ KPMG LLP

Boston, Massachusetts
March 16, 2021

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO RULE 13A-14 (A) / RULE 15D-14 (A) OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

I, Garry E. Menzel, certify that:

1. I have reviewed this Annual Report on Form 10-K of TCR2 Therapeutics Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 16, 2021

/s/ Garry E. Menzel
Garry E. Menzel
President, Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO RULE 13A-14 (A) / RULE 15D-14 (A) OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

I, Mayur (Ian) Somaiya, certify that:

1. I have reviewed this Annual Report on Form 10-K of TCR2 Therapeutics Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 16, 2021

/s/ Mayur (Ian) Somaiya
Mayur (Ian) Somaiya
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Annual Report on Form 10-K of TCR2 Therapeutics Inc. (the "Company") for the fiscal year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his or her knowledge:

1. the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 16, 2021

/s/ Garry E. Menzel
Garry E. Menzel
President, Chief Executive Officer and Director
(Principal Executive Officer)

/s/ Mayur (Ian) Somaiya
Mayur (Ian) Somaiya
Chief Financial Officer
(Principal Financial and Accounting Officer)