UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

OR

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

For the transition period from to

Commission File Number: 001-40631

Caribou Biosciences, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**45-3728228**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
2929 7th Street, Suite 105 **Berkeley, California**	**94710**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (510) 982-6030

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	CRBU	The Nasdaq Global Select Market

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

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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 Exchange Act). YES ☐ NO ☒

As of June 30, 2021, the last day of the Registrant's most recently completed second fiscal quarter, there was no public market for the Registrant's common stock. The Registrant's common stock began trading on the Nasdaq Global Select Market on July 23, 2021. The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on the Nasdaq Global Select Market on March 17, 2022, was $538,150,113. This calculation does not reflect a determination that certain persons are affiliates of the Registrant for any purpose.

The number of shares of Registrant's Common Stock outstanding as of March 17, 2022 was 60,663,581.

DOCUMENTS INCORPORATED BY REFERENCE

None

Table of Contents

Risk Factors Summary

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our common stock. These risks are more fully described in the "*Risk Factors*" section in Part I, Item 1A of this Annual Report on Form 10-K. These risks include, among others, the following:

- We have incurred significant net losses since our inception and anticipate that we will incur continued net losses for the foreseeable future.
- We will need substantial additional financing to develop our product candidates and implement our operating plans. If we fail to obtain additional financing, we may be delayed or unable to complete the development and commercialization of our product candidates.
- We have a limited operating history, which may make it difficult to evaluate our technologies and product candidate development capabilities or to predict our future performance.
- We are early in our development efforts and it will be many years before we commercialize a product candidate, if ever. If we are unable to advance our product candidates through clinical trials, obtain regulatory approval, and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.
- Our product candidates are cell therapies generated by novel CRISPR chRDNA genome-editing technologies, which make it difficult to predict the time and cost of developing these product candidates and obtaining regulatory approval. To date, no other products that use these genome-editing technologies have advanced into clinical trials or received marketing approval in the United States.
- Our business is highly dependent on the success of our product candidates, which will require significant additional preclinical studies and/or human clinical trials before we can seek regulatory approval and potentially commercialize our product candidates. If we are unable to advance our preclinical studies and clinical trials and obtain regulatory approval for, and successfully commercialize, our lead product candidates for the treatment of patients in approved indications, or if we are significantly delayed in doing so, our business will be significantly harmed.
- If we experience delays or difficulties enrolling patients in the clinical trials for our product candidates, including our ANTLER phase 1 clinical trial for our CB-010 product candidate, our ability to advance our lead and our other product candidates through clinical development and the regulatory process could be delayed or prevented.
- Our clinical trials may fail to adequately demonstrate the safety and efficacy of any of our product candidates and the development of our product candidates may be delayed or unsuccessful, which could prevent or delay regulatory approval and commercialization.
- If our product candidates cause serious adverse events or undesirable side effects, including injury and death, or have other properties that could delay or prevent regulatory approval, their commercial potential may be limited or extinguished.
- We face significant competition from other biotechnology and pharmaceutical companies, which may result in other companies developing or commercializing products before, or more successfully than, we do, thus rendering our product candidates non-competitive or reducing the size of our market. Our operating results will suffer if we fail to compete effectively.
- If we do not possess the necessary intellectual property rights covering our proprietary CRISPR chRDNA genome-editing technology and our product candidates, we may not be able to block competitors or to compete effectively in our markets.
- Third-party claims of intellectual property infringement may prevent or delay our ability to commercialize our product candidates.
- Our rights to develop and commercialize our product candidates are subject to the terms and conditions of our licenses and assignments with third parties. If we fail to comply with our obligations under these agreements, we could lose intellectual property rights and be subject to litigation from our licensors or assignors.

- Our ability to continue to receive licensing revenue and to enter into new licensing arrangements related to the foundational CRISPR-Cas9 intellectual property will be substantially impaired if such intellectual property is limited by administrative patent proceedings.
- We rely on third parties to supply the materials for, and the manufacturing of, our clinical product candidates, and, if such product candidates receive regulatory approval, we may continue our reliance on third parties for manufacturing of our commercial products.
- We may not be able to meet our obligations under the AbbVie collaboration or our own product candidates and pipeline may be delayed in light of our obligations to AbbVie. In addition, we have limited control over the achievement of milestones by AbbVie.
- Our future success depends on our ability to retain our executive officers and to attract, retain, and motivate qualified personnel.
- We have incurred, and will continue to incur, increased costs as a result of operating as a public company, and our management will continue to devote substantial time to compliance initiatives and corporate governance practices.

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

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our business strategy, plans, and objectives; expectations regarding our clinical and preclinical development programs, including our timing expectations with respect to such programs and the expected timing of disclosure of initial data from such programs; future regulatory filings; our results of operations and financial position; plans and objectives of management for future operations; and the like, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential," or "continue," or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements concerning:

- our expectations regarding the initiation, timing, progress, and results of our product candidate preclinical studies, clinical trials, and research programs including, without limitation, our timing expectations relating to the release of initial patient data from our ANTLER phase 1 clinical trial for CB-010, the submission of our IND applications for CB-011 and CB-012, and our target selection for CB-020;
- our ability to demonstrate, and the timing of, preclinical proof-of-concept *in vivo* for our product candidates;
- our ability to successfully develop our product candidates and to obtain and maintain regulatory approval for our product candidates;
- the likelihood of our clinical trials demonstrating safety and efficacy of our product candidates;
- the beneficial characteristics, therapeutic effects, and potential advantages of our product candidates;
- the timing or likelihood of regulatory filings and approval for our product candidates;
- our strategic plans for our business, product candidates, research programs, and technologies;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and genome-editing technology;
- anticipated developments related to our competitors and our industry;
- estimates regarding the sufficiency of our existing capital resources to fund our future operating expenses and capital expenditure requirements; and
- our anticipated use of our existing resources, capital requirements, and needs for additional financing.

The forward-looking statements in this Annual Report on Form 10-K are only predictions and are based largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K and are subject to a number of known and unknown risks, uncertainties and assumptions, including those described in the *"Risk Factors"* section in Part I, Item 1A of this Annual Report on Form 10-K and in the *"Management's Discussion and Analysis of Financial Condition and Results of Operations"* section in Part II, Item 7 of this Annual Report on Form 10-K. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or may not occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in a very competitive and rapidly evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

PART I

Item 1. Business.

Overview

We are a clinical-stage genome-editing biopharmaceutical company dedicated to developing transformative CRISPR therapies for patients with devastating diseases. CRISPR is an acronym for **C**lustered **R**egularly **I**nterspaced **S**hort **P**alindromic **R**epeats. Our novel CRISPR platform, **C**RISPR **h**ybrid **R**NA-**DNA** ("chRDNA," pronounced "chardonnay"), enables superior genome-editing precision to develop cell therapies that are specifically engineered for enhanced persistence. We are advancing a pipeline of allogeneic, or off-the-shelf, chimeric antigen receptor ("CAR")-T ("CAR-T") and CAR-natural killer ("CAR-NK") cell therapies for the treatment of patients with hematologic malignancies and solid tumors. Our renowned founders, including a Nobel laureate, are pioneers in the field of CRISPR genome editing. Our chRDNA technology has demonstrated superior specificity and high efficiency in preclinical studies and enables us to perform multiple, precise genome edits, while maintaining genomic integrity.

We believe that our technology has broad potential to generate gene and cell therapies in oncology and in therapeutic areas beyond oncology. Potential applications include immune cell therapies, cell therapies derived from genome-edited induced pluripotent stem cells ("iPSCs"), and *in vivo* genome-edited therapies.

The genome-editing technologies currently used in the allogeneic cell therapy field generally have limited efficiency, specificity, and versatility for performing the multiple, precise genomic edits necessary to address insufficient persistence. Our CRISPR chRDNA technology is designed to address these genome-editing limitations and improve cell therapy activity. By applying our approach to allogeneic cell therapies, we believe we can unlock their full potential by improving upon their effectiveness and durability.

We are initially focused on advancing multiple proprietary allogeneic cell therapies for the treatment of both hematologic malignancies and solid tumors against cell surface targets for which autologous CAR-T cell therapeutics have previously demonstrated clinical proof of concept, including CD19 and B cell maturation antigen ("BCMA"), as well as other targets. We use our chRDNA technology to enhance, or armor, our cell therapies with multiple strategies, such as checkpoint disruption and immune cloaking, to improve persistence of antitumor activity.

Our lead product candidate, CB-010, is, to our knowledge, the first clinical-stage allogeneic anti-CD19 CAR-T cell therapy with programmed cell death protein 1 ("PD-1") removed from the CAR-T cell surface by a genome-edited knockout of the *PDCDI* gene. We have demonstrated in preclinical models that the PD-1 knockout improves the persistence of antitumor activity by disrupting a pathway that leads to rapid T cell exhaustion. CB-010 is being evaluated in our ANTLER phase 1 clinical trial in patients with relapsed or refractory B cell non-Hodgkin lymphoma ("r/r B-NHL"). We expect to disclose initial clinical data from this trial at a medical conference in 2022.

Our CB-011 product candidate is an allogeneic CAR-T cell product candidate that is, to our knowledge, the first anti-BCMA CAR-T cell therapy incorporating an immune cloaking approach that includes both the removal of the endogenous beta-2 microglobulin ("B2M") protein and insertion of a beta-2-microglobulin–human-leukocyte-antigen-E–peptide transgene ("B2M–HLA-E"). This strategy is designed to blunt CAR-T cell rejection by both patient T cells and natural killer ("NK") cells to enable more durable antitumor activity. CB-011 is in preclinical development for relapsed or refractory multiple myeloma ("r/r MM"). We expect to submit an investigational new drug ("IND") application for CB-011 in 2022.

CB-012 is our allogeneic armored CAR-T cell product candidate targeting CD371, currently in preclinical development for the treatment of relapsed or refractory acute myeloid leukemia ("r/r AML"). We expect to submit an investigational new drug ("IND") application in 2023. CD371 is an attractive target for AML due to its expression on myeloid cancer cells, its enrichment in leukemic stem cells, and its absence on hematopoietic stem cells.

We are also developing allogeneic CAR-NK cell therapies derived from genome-edited iPSCs for the treatment of solid tumors. CB-020 is our first CAR-NK product candidate and it will contain genomic edits designed to overcome some of the challenges of targeting solid tumors, such as trafficking, tumor infiltration, heterogeneity, and the immunosuppressive tumor microenvironment. We expect to select a tumor cell-surface target for our CB-020 product candidate in 2022.

We control a robust patent portfolio protecting our chRDNA technology as well as certain single-chain variable fragments ("scFvs") used in our product candidates.

In February 2021, we entered into a Collaboration and License Agreement (the "AbbVie Agreement") with AbbVie Manufacturing Management Unlimited Company ("AbbVie") to develop two new CAR-T cell therapies for AbbVie. We view this collaboration as an external recognition of the potential for our Cas12a chRDNA genome-editing technology to significantly improve genome-editing specificity and efficiency.

Our team and our culture are critical to realizing our vision of advancing agile genome-editing innovations for the benefit of our communities. We were founded in 2011 by globally-recognized leaders in CRISPR genome editing and nucleic acid biology: Jennifer A. Doudna, Ph.D., who was a co-recipient of the 2020 Nobel Prize in Chemistry for the development of CRISPR-Cas9 as a method for genome editing; Martin Jinek, Ph.D., Assistant Professor at the University of Zurich in the Department of Biochemistry; James Berger, Ph.D., Professor in the Department of Biophysics and Biophysical Chemistry at the Johns Hopkins University School of Medicine; and Rachel E. Haurwitz, Ph.D., who has served as our president and chief executive officer since our formation. Drs. Doudna and Jinek serve on our scientific advisory board ("SAB"), which also includes world experts in immunotherapies, T cell metabolism and tumor interactions, iPSC biology and differentiation, clinical trial development, and patient care. Our current team of employees includes scientists who invented the technologies we use today in our research and product development, including our chRDNA genome-editing technology, and who continue to drive innovation.

Our mission is to develop innovative, transformative therapies for patients with devastating diseases through novel genome editing. To support this mission, we have developed the following values to guide our employees:

- *Innovation is in our chRDNA*
- *Together we are stronger*
- *Integrity and ethics guide our decision making*
- *We are driven by patient need*

Genome-Editing Landscape and Limitations

Genome editing is a class of technologies that facilitate making specific changes to DNA sequences inside living cells. Genome editing occurs in two steps, as shown in figure 1 below. In the first step, a double stranded break ("DSB") is made at the location of the genome where the edit is desired. A cell typically has two ways to repair the DSB, which result in the knockout of a gene or the insertion of new genetic material: non-homologous end joining ("NHEJ") and homology-directed repair ("HDR"). NHEJ is an error-prone process in which the broken DNA ends are reattached. During NHEJ, the cell typically inserts or deletes a few nucleotides at the DSB. These insertions and deletions ("indels") destroy the coding sequence for the targeted gene, resulting in the knockout of the targeted sequence. HDR, by contrast, is a more controlled repair system where the cell incorporates donor DNA delivered during the experiment into the DSB, resulting in the site-specific insertion of the provided DNA sequence.

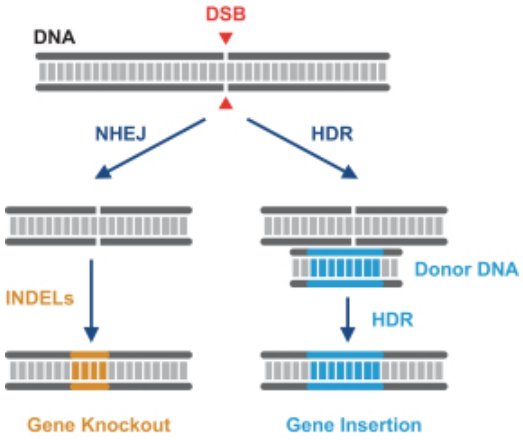


Figure 1. *Genome editing is initiated by generating a double-stranded break in chromosomal DNA at a desired location. The cell will seal the break by an error-prone process called non-homologous end joining, leading to the formation of insertions and deletions, resulting in a site-specific gene knockout. If a donor DNA template is provided to the cell during genome editing that encodes a gene of interest, a process called homology-directed repair will result in the insertion of the donor DNA in a site-specific manner.*

There are several well-established genome-editing technologies being applied to generate immune cell therapies currently in preclinical research or clinical development, including zinc-finger nucleases ("ZFNs"), transcription activator-like effector nucleases ("TALENs"), and meganucleases, but each has limitations with respect to both their agility and their ability to generate site-specific gene insertions with high efficiency. More recently, CRISPR genome-editing technology has been used for the generation of *ex vivo* immune cell therapeutics that are in preclinical research or clinical development.

The canonical CRISPR system utilizes Cas9, a protein that can cut genomic DNA. Cas9 is targeted to a specific site in a genome by a guide RNA. One of the drawbacks of CRISPR-Cas9 genome editing is the occurrence of off-target editing. Off-target edits can alter an oncogene or tumor suppressor gene, impact the biology of the target cell, or have other negative consequences on therapeutic development. Additionally, the simultaneous occurrence of both on-target and off-target edits may lead to genomic rearrangements including chromosomal translocations that may be problematic for immune cell therapeutics, especially for ones requiring multiple edits.

Our CRISPR Hybrid RNA-DNA (chRDNA) Technology

Overview

We employ a new CRISPR genome-editing platform, our chRDNA technology, which uses novel and proprietary hybrid guides for editing DNA, providing a powerful tool with the potential to expand the use of allogeneic cell therapies. The advantages of our chRDNA technology include:

- *Significantly improved genome-editing specificity:* The use of our chRDNA guides leads to a high degree of editing specificity with lower levels of off-target events compared to first generation CRISPR-Cas9 or CRISPR-Cas12a using all-RNA guides. See figure 2 below.
- *High efficiency:* We achieve a high degree of on-target gene knockout and insertion efficiency, facilitating robust multiplex editing including multiple gene insertions. See figure 2 below.
- *Versatility across a broad range of cell types:* Our chRDNA guides are compatible with multiple types of Cas proteins, including Cas9 and Cas12a, providing us the flexibility to apply our technology to many cell types including immune cells and stem cells.
- *Simple chemical synthesis:* Our chRDNA guides are manufactured via chemical synthesis using readily available technologies.

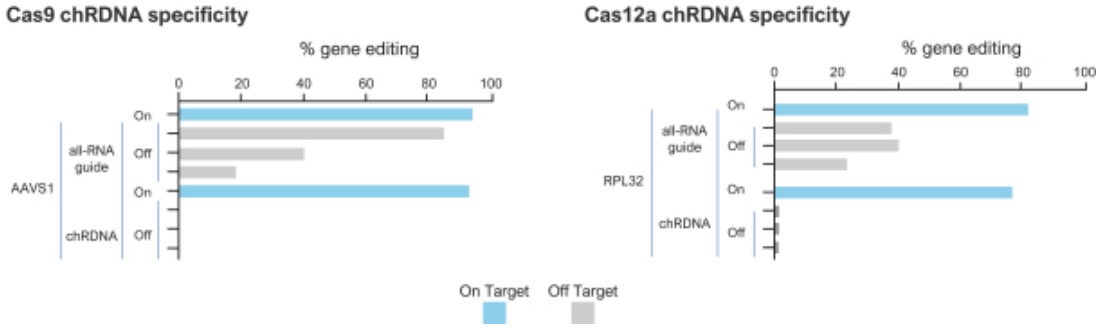


Figure 2. *chRDNA guides significantly improve genome-editing specificity relative to all-RNA guides. We edited the AAVS1 and RPL32 genes using either an all-RNA guide or a chRDNA guide targeting the same genomic location and the all-RNA guides result in multiple, high efficiency off-target edits, whereas the chRDNA guides yield minimal or undetectable off-target edits.*

Our chRDNA Guides

Our chRDNA technology uses the canonical *S. pyogenes* Cas9 protein or the *Acidaminococcus sp.* Cas12a protein and a guide that is composed of a mixture of RNA and DNA nucleotides in both the region that interacts with the chromosomal target DNA and in the region that does not interact with the target DNA. See figure 3 below. The presence of DNA in a chRDNA guide

significantly improves editing specificity relative to an all-RNA guide. Like Cas9, Cas12a is a CRISPR protein used to edit genomic DNA site-specifically. See figure 4 below. We have developed the chRDNA guides to achieve the following advantages:

- Significantly improved genome-editing specificity;
- High-efficiency gene knockouts and insertions, with Cas12a chRDNA-mediated editing driving high-efficiency gene insertions; and
- Versatility across broad range of cell types and simple chemical synthesis.

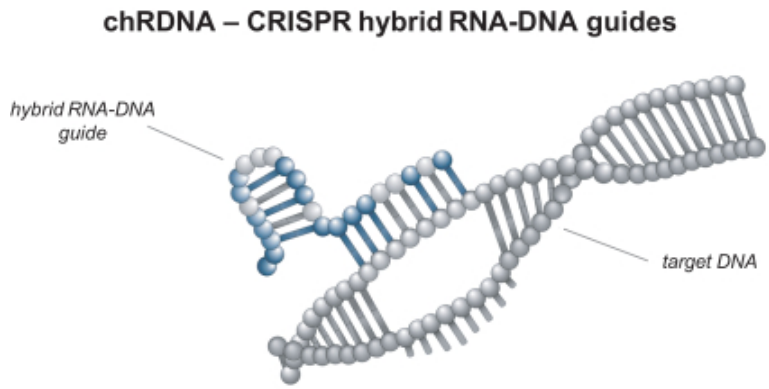


Figure 3. *Our chRDNA guides are hybrid molecules that contain both RNA and DNA nucleotides. They enable significantly improved specificity compared to first generation all-RNA guides.*

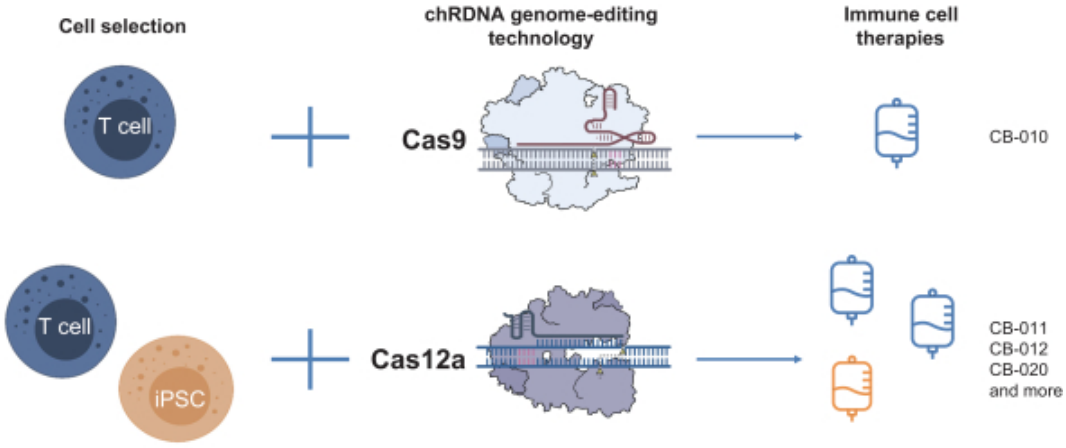


Figure 4. *We use Cas9 and Cas12a in the development of our allogeneic cell therapies.*

Our chRDNA Guides: Highly Specific On-Target Genome Editing

Our chRDNA guides mediate higher genome editing specificity as compared to all-RNA guides. For Cas9 chRDNA guides, we have demonstrated that the presence of DNA in our chRDNA guides improves the specificity of genome editing by decreasing the affinity of a Cas9 chRDNA complex for off-target sites, and we hypothesize that similar properties enable high specificity editing for Cas12a chRDNA guides. A chRDNA guide retains sufficiently high affinity to edit a genome at the intended location. However, a chRDNA guide has sufficiently low affinity for potential off-target sites to reduce the likelihood of a genome edit at an unintended location. We evaluated the integrity and performance of chRDNA guides by employing two proprietary assays, the SITE-Seq® assay and the VINE methodology, on two genes known from the scientific literature to suffer from high rates of off-target editing with either the Cas9 or Cas12a protein. As seen in figure 5 below, all-RNA guides generated both robust on-target and off-target editing. We developed chRDNA guides that target the exact same genomic locations that achieve equivalent on-target editing compared to the all-RNA guides. However, the chRDNA guides, in contrast to the all-RNA guides, result in little to no detectable off-target editing. For any single genome edit, the chRDNA platform provides high specificity for use in our product candidates. We have generated chRDNA guides for Cas9 and for Cas12a targeting multiple distinct locations in the human primary T cell genome that lead to high

efficiency and high specificity editing. We recently published an article in *Molecular Cell*, a peer-reviewed journal, on the mitigation of off-target editing using Cas9 chRDNAs (Donohoue, P.D. *et al.*, *Molecular Cell* 81, 3637–3649, September 2, 2021). Figure 5 below shows the increased editing specificity with Cas9 and Cas12a chRDNA guides.

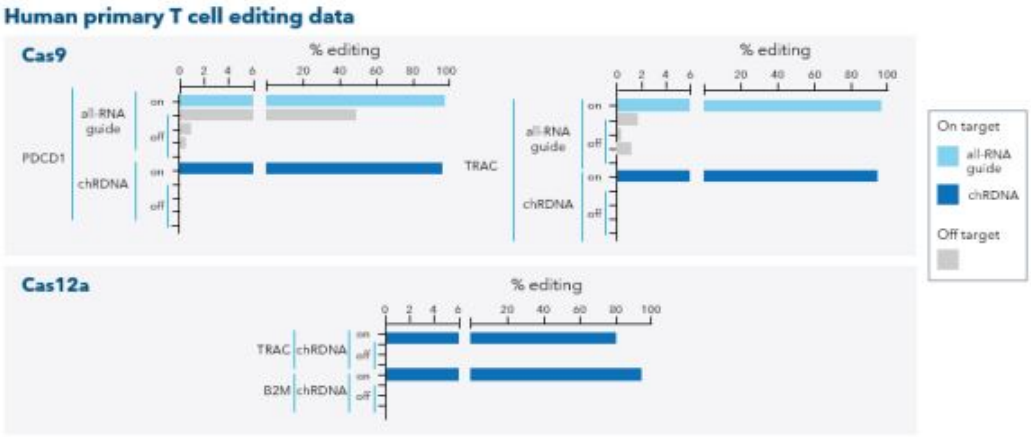


Figure 5. *Our chRDNA guides yield significantly increased editing specificity compared to all-RNA guides with either Cas9 or Cas12a.*

Our chRDNA Guides: Achieve Equivalent, High Gene Knockout Efficiencies Compared to Conventional all-RNA Guides

The inclusion of DNA in our chRDNA guides does not impair their activity, and they achieve knockout efficiencies in human primary T cells with either the Cas9 or Cas12a protein that are equivalent to the knockout efficiencies achieved with all-RNA guides.

Our chRDNA Guides: Cas12a chRDNA-Mediated Editing Drives High Efficiency Gene Insertions

One of the challenges in the genome-editing field is obtaining a high degree of site-specific gene insertion. High efficiency gene knockout is achievable with a variety of genome-editing technologies, but achieving high efficiency gene insertion is more challenging. Either Cas9 or Cas12a can be used to insert a new gene into a genome. We use the combination of the Cas12a protein and our chRDNA guides to generate particularly high and reproducible gene insertion rates. Gene insertion requires delivery of the new gene into the target cells. To insert genes into T cells with our chRDNA technology, we transduce the cells with an engineered adeno-associated virus serotype 6, or AAV6, which contains the DNA template of interest to facilitate the integration of the DNA into the double-stranded break generated by the Cas9 chRDNA complex or the Cas12a chRDNA complex via the homology-directed repair pathway.

As shown in figure 6 below, approximately 63-86% gene insertion rates were achieved in human primary T cells edited with Cas12a chRDNAs, a significant rate that is competitive with other genome-editing platforms. We demonstrated the insertion of a BCMA-specific CAR transgene, or Insert 1, into the *TRAC* locus by staining the edited T cells for the expression of the CAR following the knockout of the T cell receptor ("TCR"), via a *TRAC* knockout, and the insertion of the CAR transgene into the *TRAC* locus. In the same T cells, we demonstrated the insertion of a B2M–HLA-E fusion gene, or Insert 2, into the B2M locus by staining the edited T cells for the expression of HLA-E following the knockout of all class I antigens via a B2M knockout and the insertion of the B2M–HLA-E fusion gene into the B2M locus. In the same T cells, Cas12a chRDNA-mediated gene insertion rates are sufficiently high to enable multiplex insertions in the manufacture of some of our product candidates. For example, we implement two separate

insertions in the manufacture of CB-011: an insertion of the BCMA-specific CAR transgene into the *TRAC* locus and an insertion of the B2M–HLA-E fusion gene into the B2M locus.

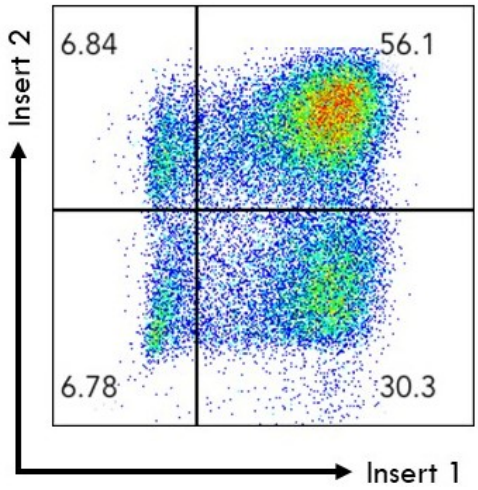


Figure 6. *Our Cas12a chRDNA technology mediates high rates of site-specific insertion. High efficiency Cas12a chRDNA editing yields ~56% of the modified T cells possessing 2 gene inserts and 2 gene knockouts, thus all 4 desired edits.*

Our chRDNA Guides: Capable of Multiplex Editing with Reduced Risk of Chromosomal Translocations via Our Proprietary Delivery Technology

By combining our chRDNA guides together with our proprietary delivery technology, we believe we are positioned to generate immune cell therapy product candidates with a higher degree of genomic integrity. High genomic integrity is crucial to ensuring that patients are not infused with immune cells harboring the potential for tumorigenicity or that have impaired function. The cell therapy product candidates we are developing include multiple genetic changes. For example, the CB-010 product candidate has edits at both the *TRAC* and *PDCD1* genes. In an effort to maintain the genomic integrity of our T cells after multiple editing events, we employ a proprietary delivery technology that relies on delivery parameters via electroporation for the introduction of Cas proteins and chRDNA guides into human primary T cells. Through this delivery technology, we minimize the generation of chromosomal translocations and genomic rearrangements that may result from multiple genome edits. Multiplex editing in T cells with different genome-editing technologies, such as TALENs or CRISPR-Cas9, using standard delivery technologies leads to 2-5% of the T cells containing chromosomal translocations or other genome rearrangements. As shown in figure 7 below, using the standard electroporation delivery technology commonly utilized for *ex vivo* cell therapy manufacturing, >3% translocation rates were observed when performing two genome edits. In contrast, when using our proprietary delivery technology, the translocation rate is more than an order of magnitude less, at 0.1%.

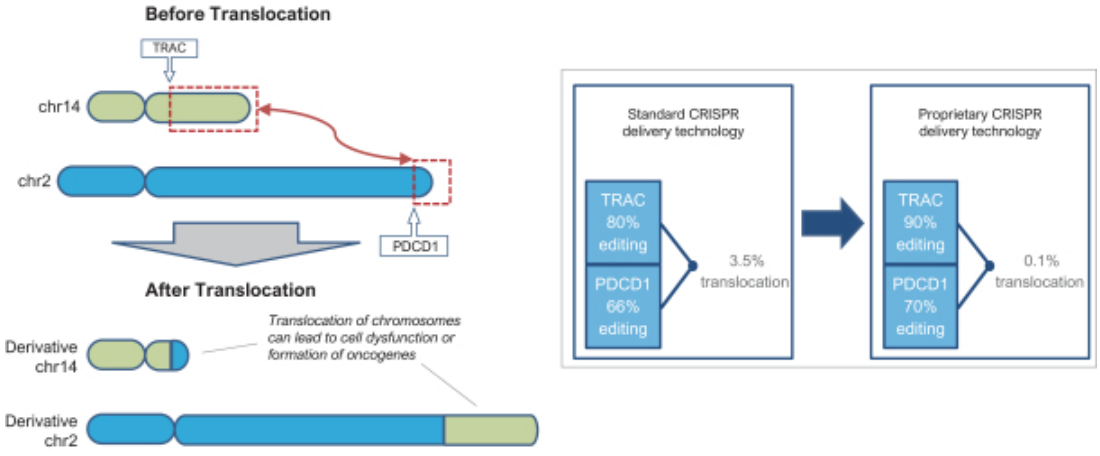


Figure 7. *Our proprietary delivery technology maintains the genomic integrity of our cellular therapies by significantly reducing the rates of chromosomal translocations.*

Immune Cell Therapies

Overview

Immune cell therapies have emerged as a revolutionary and potentially curative treatment for hematologic malignancies and solid tumors. The approval and commercialization of multiple first-generation CD19- and BCMA-directed autologous CAR-T cell products have laid the foundation and opened a path for the development of more advanced cell therapeutics, including CAR-T and CAR-NK cell products with next-generation capabilities and approaches. Among these approaches, allogeneic cell therapy is positioned to unlock the broad potential of genome-edited immune cells as a leading therapeutic modality. However, expansion, persistence, and trafficking of allogeneic CAR-T and CAR-NK cells are critical to achieving long-term efficacy. We believe that the genome-editing technologies currently utilized in the allogeneic cell therapy field have limited efficiency, specificity, and versatility for performing the multiplex editing necessary to address these challenges.

Within the immune system, white blood cells, such as T cells and NK cells, are responsible for defending the body against not only pathogens but also abnormal cells, including cancer cells. Receptors on the surface of T cells enable them to recognize tumor cells and coordinate the activation of other cells in an immune response leading to the destruction of the cancerous cells. However, in many cases, cancer-specific T cells are not present in sufficiently high numbers or do not have the appropriate tumor specificity in a patient to eliminate a tumor.

Autologous immune cell therapies, the most advanced of which use T cells, are a class of therapies in which immune cells are removed from a patient's body and modified to express CARs. CARs are engineered molecules that, when present on the surface of an immune cell, enable the immune cell to recognize specific proteins, or antigens, that are present on the surface of other cells, including cancer cells. To manufacture autologous CAR-T cell therapies, a cancer patient's own T cells are modified to express a particular CAR, grown outside the patient's body to expand their numbers, and then infused back into the same patient to recognize and destroy cancer cells in a targeted manner.

Allogeneic Cell Therapies

Despite the successes of autologous CAR-T cell therapies, several limitations have prevented autologous therapies from achieving the full potential of CAR-T products:

- *Limited patient access.* Many patients are not eligible for autologous therapy because of the quality of their T cells or the lengthy vein-to-vein time.
- *Bridging therapy often required.* Long wait times between the initial collection of the patient's T cells and the return of the modified cells back to the patient often require an intervening additional line of therapy, also known as bridging therapy.
- *Manufacturing complexity.* Autologous cell manufacturing is complex and lengthy and there are occasional manufacturing failures. The consequence of a manufacturing failure is that a patient might never receive their treatment.
- *High production costs.* Due to the personalized nature of autologous therapy, only one patient can be treated from each manufacturing run; the supply chain logistics, including manufacturing and delivery, result in high costs with limited ability to scale.
- *Variable potency*. Often patients' T cells may be damaged and weakened due to prior cancer treatments, which may lead to variable potency of the manufactured T cells and variability in outcomes of the therapy.

Universal off-the-shelf, or allogeneic, versions of CAR-T or CAR-NK cells derived from healthy donors are attractive options for several reasons.

- *Broad patient access.* Allogeneic therapies derived from healthy donor cells have the potential to provide therapeutic options for patients who are ineligible for autologous CAR-T cell treatments due to the condition of their T cells. Patients whose disease requires more immediate treatment and who cannot wait for autologous CAR-T cell therapy will benefit from allogeneic cell therapies.

- *Bridging therapy not required.* This contrasts with autologous cell therapy, as patients may require bridging therapy to treat their cancer from the time their cells are collected until their CAR-T cell therapy is manufactured and administered.

- *Off-the-shelf availability.* Allogeneic CAR-T cells are manufactured in advance, are stored in inventory, and are available for any eligible patient at any time. Compared to autologous therapies, there is a significantly shortened waiting time, without the need for bridging therapy. In addition, allogeneic cell therapies may offer an opportunity for repeated dosing in patients with significant tumor burden.

- *More efficient and cost-effective manufacturing.* Allogeneic approaches utilize cells from healthy donors resulting in a streamlined manufacturing process, enhanced scalability, and cost reduction.

- *Healthy donor cells genome-engineered for potency and persistence*. Allogeneic therapies are produced from selected and screened T cells of healthy donors resulting in enhanced cell consistency, potency, and potentially more predictable treatment outcomes.

Although allogeneic cell therapy is positioned to unlock the broader potential of engineered immune cells as a leading therapeutic modality, it has not yet achieved the efficacy of autologous therapies. We believe that the expansion and persistence of allogeneic CAR-T cells are critical to achieving long-term efficacy. Unlike autologous CAR-T cell therapies, allogeneic CAR-T cell therapies are prone to rapid rejection by a patient's immune system, thus limiting antitumor activity. Additionally, CAR-T cell therapies have not demonstrated significant and reproducible efficacy in solid tumors to date. While multiple CAR-T cell approaches are being evaluated in clinical trials for the treatment of solid tumors, the efficacy observed to date is limited and lower than that observed when treating hematologic malignancies. This may be due to poor CAR-T cell trafficking and infiltration into tumors and metastases, and their limited antitumor function within the immunosuppressive tumor microenvironment.

Our Strategy

Key Components of our Strategy

Our purpose is to develop transformative genome edited-based therapies for devastating human diseases. Our goal is to build an integrated company that discovers, develops, manufactures, and commercializes genome edited therapies that hold the potential to significantly impact a wide range of diseases.

Key components of our strategy include:

- *Applying our chRDNA platform to develop allogeneic CAR-T cell therapies designed for improved persistence through diverse armoring strategies.* We are advancing clinical development of our lead product candidate, CB-010, for r/r B-NHL as well as research and development for our preclinical product candidate, CB-011, for r/r MM. CB-010 is directed to the CD19 target, and CB-011 is directed to the BCMA target. These targets have been clinically validated in the autologous CAR-T cell therapeutic setting, providing us appropriate indications with limited target risk in which to evaluate the role of enhanced allogeneic CAR-T cell antitumor persistence. CB-010 is being evaluated in our ANTLER phase 1 clinical trial and we expect to disclose initial clinical data from this trial at a medical conference in 2022.

- *Developing additional allogeneic CAR-T cell product candidates for the treatment of hematologic malignancies.* Immune cell therapies have emerged as an exciting and powerful approach for difficult-to-treat hematologic malignancies in patients with limited treatment options. We are applying our chRDNA platform and insights from our more developed programs to create allogeneic CAR-T cell therapies against targets for diseases such as AML, and we plan to use multiple armoring strategies to enhance the persistence and efficacy of our product candidates.

- *Expanding our cell therapy pipeline to include cell therapies for the treatment of solid tumors and metastases by leveraging our iPSC-derived NK cell ("iNK") therapy platform.* We believe NK cells are a promising cell type for the treatment of solid tumors and metastases. We have developed the ability to edit iPSCs and differentiate them into NK cells that have antitumor potential. We intend to pursue targeting multiple types of solid tumors for which there is high unmet medical need.

- *Reinforcing our leadership in CRISPR genome editing through strategic investments in our platform and new technologies.* Our company was founded by leaders in CRISPR biology and its development for use as a platform to generate therapeutics. Our foundation is based on science and innovation protected by a robust IP portfolio and we will continue to invest in and build up these areas to maintain our prominence in the field and to develop therapies in which our genome edits confer potential benefits to patients.

- *Further expanding patient access to our cell therapies via selective strategic collaborations, such as our collaboration with AbbVie.* We executed a strategic license and collaboration agreement with AbbVie in February 2021 to develop two allogeneic CAR-T cell therapies for AbbVie using our Cas12a chRDNA genome-editing and cell therapy technologies. In the future, we may seek additional opportunities with select collaborators as appropriate to accelerate our ability to develop therapeutics to address significant unmet medical need.

- *Pursuing indications both within and outside of oncology on our own and through selective strategic collaborations.* We believe that our technology has broad potential to generate gene and cell therapies in oncology and in therapeutic areas beyond oncology. Potential applications include immune cell therapies, cell therapies derived from genome-edited iPSCs, and *in vivo* genome-edited therapies. We aspire to maximize the value of our technologies and capabilities for patient benefit through internal investment and development and through collaborations.

Multiplex Genome Editing Strategy Using our chRDNA Technology

We have successfully demonstrated multiplex genome editing with our chRDNA technology, including multiplex gene insertion. We believe this level of editing sophistication has the potential to unlock the broad use of allogeneic cell therapies by:

- *Increasing the persistence of allogeneic cell therapies, thereby potentially achieving long-term efficacy:* Our chRDNA technology enables us to apply multiple orthogonal approaches to armor allogeneic CAR-T cells, including (i) checkpoint disruption, through a knockout of PD-1 to sustain the initial activity of CAR-T cells by disrupting a pathway that leads to CAR-T cell exhaustion and (ii) immune cloaking of CAR-T cells to prevent rapid rejection by the patient's immune system. See figure 8 below. Our preclinical mouse xenograft data demonstrate that the PD-1 knockout results in a significant survival advantage compared to conventional allogeneic CAR-T cells without a PD-1 knockout. See figure 9 below.

- *Improving the genomic integrity of our products*: We have observed that our product candidates have significantly lower levels of off-target edits compared to those made with first generation CRISPR-Cas9, and we believe we can make multiple edits while maintaining genomic integrity.

- *Expanding into solid tumors:* We are also focused on developing genome-edited, off-the-shelf CAR-NK cell therapies for the treatment of solid tumors. In our studies to date, we have observed that our chRDNA technology can precisely edit iPSCs and through a proprietary process, we generate genome-edited iNKs that are armored to enhance efficacy, trafficking, targeting, and/or persistence.

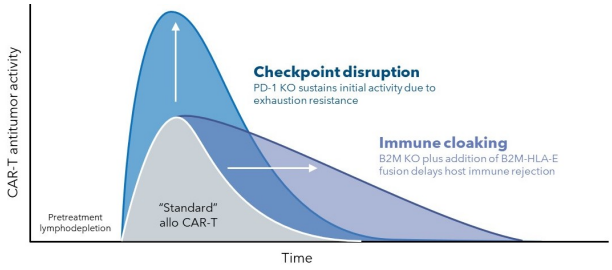


Figure 8. *We employ multiple armoring strategies to improve allogeneic CAR-T cell persistence.*

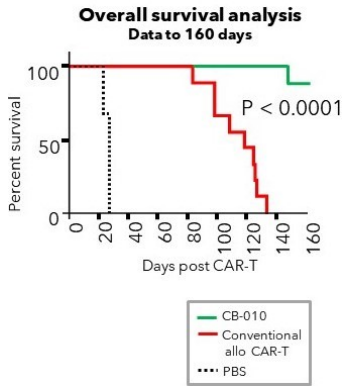


Figure 9. *In vivo preclinical mouse xenograft data demonstrate that the PD-1 knockout results in a significant survival advantage relative to a conventional allogeneic CAR-T cell therapy that expresses PD-1.*

Persistence is the Key to Unlocking the Full Potential of Allogeneic Cell Therapies

We believe greater persistence is necessary for the realization of the full potential of allogeneic cell therapies, as shown in figure 8 above. CAR-T cells will generally proliferate in response to tumor antigen engagement via their respective CAR. However, allogeneic CAR-T cells are rapidly rejected by a patient's immune system due to their genetically divergent donor-derived immune profile.

Data from patients treated with autologous CAR-T cell therapies suggest that sustained, longer-term remission is associated with the persistence of CAR-T cells. We believe that allogeneic cell therapies must persist in either their antitumor activity before exhaustion or remain in circulation within a patient's bloodstream and lymphatics for an extended period, or both, to meaningfully compete with the response rates of autologous cell therapies.

Development of an allogeneic CAR-T cell therapy requires genome editing to remove proteins from donor T cells that may recognize and attack a patient's tissue that, without removal, would pose a risk of graft versus host disease ("GvHD"). Furthermore, the donor T cells will express surface proteins that signal that they are "foreign" to the patient's immune system such that they are rapidly rejected by the patient's immune system. We believe allogeneic CAR-T cells must be modified via genome editing to enable them to safely and sufficiently persist to provide therapeutic benefit to rival the response rates of autologous CAR-T cells.

Our Approach: Armoring Cell Therapies to Increase the Persistence of Antitumor Activity

We believe that improving CAR-T cell persistence is the key to long-term efficacy in the allogeneic setting. Our strategy to improve CAR-T cell persistence is two-fold: (i) checkpoint disruption, through a knockout of PD-1 to sustain the activity of CAR-T cells by disrupting a pathway that leads to CAR-T cell exhaustion and (ii) immune cloaking the CAR-T cells to prevent rapid rejection by the patient's immune system. Similar strategies may be used for our CAR-NK platform where persistence will be key for long-term duration of antitumor activity.

Checkpoint Disruption with PD-1 Knockout Strategy

One of the approaches we deploy to increase the persistence of CAR-T cell antitumor activity is to remove PD-1 from the CAR-T cell surface. The PD-1/PD-L1 pathway leads to rapid exhaustion in T cells. This occurs when a T cell expressing PD-1 engages with another cell expressing PD-L1. Tumor cells and the patient's own cells can express PD-L1, leading to interaction with PD-1 and subsequent exhaustion of the CAR-T cells. We use our chRDNA technology to knock out the PD-1 gene and eliminate PD-1 expression from the CAR-T cell surface, thereby preventing PD-1/PD-L1-mediated exhaustion. We believe that knocking out PD-1 will maintain the CAR-T cells in a higher antitumor state for a longer period of time, and we believe this will result in greater initial tumor debulking in the patient which may lead to long-term durability of CAR-T cell antitumor activity. As shown in figure 9 above, our preclinical *in vivo* data from experiments conducted in mouse xenograft models submitted as part of our CB-010 IND application demonstrate that knocking out PD-1 leads to a significant increase in the durability of antitumor activity and therefore overall mouse survival. To our knowledge, our CB-010 product candidate is the first allogeneic CAR-T cell therapy in a clinical study with a PD-1 knockout, and we believe the PD-1 knockout will drive the durability of allogeneic CAR-T cell antitumor activity.

Immune-Cloaking Strategy

Another approach we deploy to increase the persistence of CAR-T cell antitumor activity is to immune cloak our CAR-T cells to prevent rapid immune-mediated rejection. The goal of immune cloaking is to maintain the allogeneic CAR-T cells in circulation for a longer period of time. Allogeneic CAR-T cells are foreign to the patient's immune system and, unless modified, will be rapidly rejected. We use our Cas12a chRDNA technology to make multiple edits to T cells to immune cloak them and prevent rapid rejection by both the patient's cytotoxic T cells and NK cells. Our edits remove all endogenous HLA class I antigens from the CAR-T cell surface and lead to the overexpression of HLA-E, a minor antigen, on the CAR-T cell surface. The lack of endogenous HLA class I antigens and the presence of only HLA-E are designed to prevent the patient's T cells and NK cells from rapidly rejecting the allogeneic therapy. These cells are unlikely to persist indefinitely, and ultimately other types of immune cells in the patient will eliminate the allogeneic CAR-T cells. Our edits are designed to maintain the CAR-T cells in circulation longer to promote the persistence of the CAR-T cell therapy to destroy a larger proportion of the targeted tumor cells.

Our Pipeline

We are advancing a pipeline of allogeneic CAR-T and CAR-NK cell therapies, initially focused on the treatment of patients with hematologic malignancies and solid tumors. Additionally, under the AbbVie collaboration, we are developing two new CAR-T cell therapies for AbbVie. Our pipeline is set forth in figure 10 below.

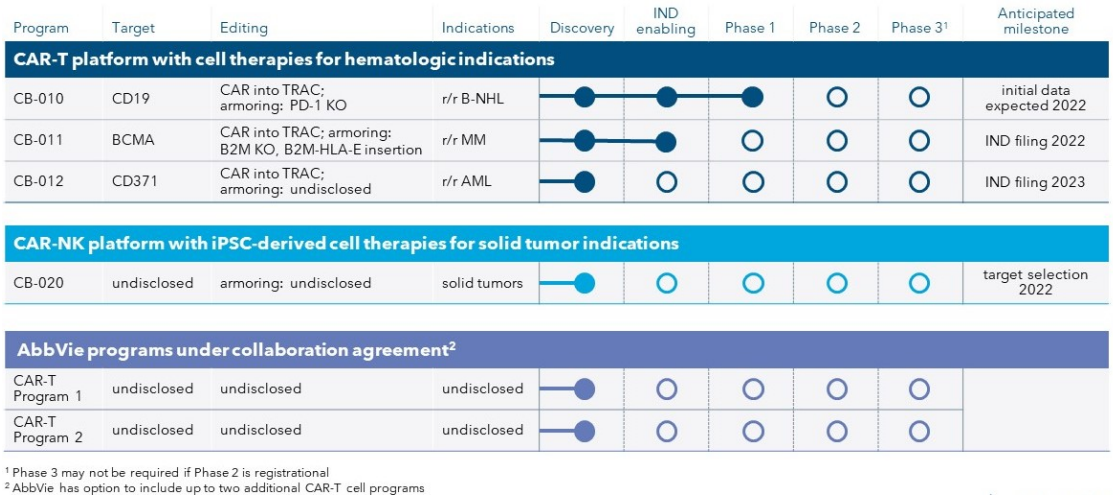


Figure 10. *Caribou is developing a robust pipeline with an initial focus on allogeneic cell therapy programs for hematologic malignancies and solid tumors.*

CB-010

Overview: Strategy and Rationale

Our lead product candidate is CB-010, a healthy donor-derived, genome-edited, allogeneic CAR-T cell therapy targeting CD19-positive malignancies, that is being evaluated in the first-in-human, open-label, multicenter ANTLER phase 1 clinical trial (NCT04637763) in the United States in adults with r/r B-NHL. CB-010 is designed to prevent rapid CAR-T cell exhaustion and confer a better therapeutic index compared to other allogeneic CAR-T cells. To manufacture CB-010, we make three modifications to healthy donor-derived T cells using our Cas9 chRDNA genome-editing technology:

- *TRAC knockout:* We knock out the *TRAC* gene in order to eliminate expression of the TCR from the surface of the CAR-T cells. The removal of TCR expression is intended to eliminate the risk of GvHD in patients.
- *Site-specific insertion of the anti-CD19 CAR:* We insert the CD19-targeted CAR into the *TRAC* gene by AAV6 transduction and homology directed repair. We believe site-specific insertion of the CAR has advantages compared to random integration mediated by lentiviral or retroviral insertion. For example, random integration leads to the risk of

unintended gene disruption which is avoided via site-specific insertion. The insertion of the CAR yields a cell therapy product candidate that exhibits CD19-specific cytotoxicity.

- *PD-1 knockout:* We knock out the gene *PDCDI*, which encodes for PD-1, a checkpoint receptor, to improve the persistence of CAR-T cell antitumor activity.

The PD-1/PD-L1 pathway leads to rapid exhaustion in T cells. This occurs when a T cell expressing PD-1 engages with another cell expressing PD-L1. B cell tumors and the patient's own cells can express PD-L1, leading to interaction with PD-1 and subsequent exhaustion of the CAR-T cells. We eliminate PD-1 expression from the CB-010 CAR-T cells, thereby preventing PD-1/PD-L1-mediated exhaustion. More than half of B-NHL tumors express PD-L1, and expression of PD-L1 in B-NHL correlates with poorer outcomes. We believe that knocking out PD-1 will maintain the CAR-T cells in a higher antitumor state for a longer period of time, and we believe this will result in greater initial tumor debulking in the patient and thereby better long-term durability of the CAR-T cell antitumor activity. To our knowledge, CB-010 is the first allogeneic CAR-T therapy in the clinic with a PD-1 knockout. Other CAR-T cell therapies that express endogenous PD-1 could become rapidly exhausted and lose antitumor activity due to the interaction between PD-1 and PD-L1.

Figure 11 below graphically depicts CB-010 CAR-T cells lacking expression of PD-1 interacting with a CD19-expressing tumor cell that expresses PD-L1 on its surface. The lack of interaction between PD-L1 on a tumor cell and the CB-010 CAR-T cell eliminates the induction of the PD-1 checkpoint pathway in the T cells that would otherwise lead to their exhaustion.

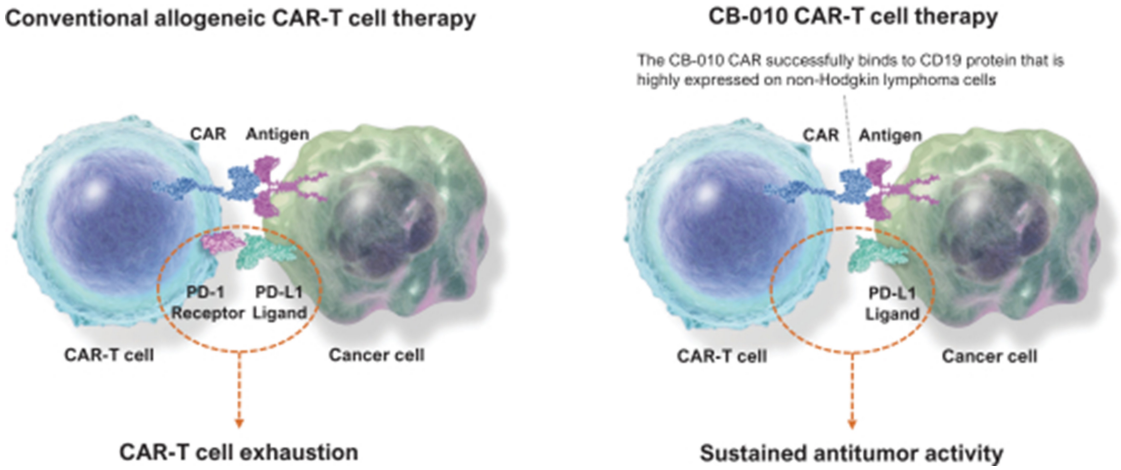


Figure 11. *Cancer cells use the PD-1/PD-L1 signaling pathway to evade immune cells and avoid destruction. The PD-L1 ligand on the tumor cell surface binds to the PD-1 receptor on the conventional allogeneic CAR-T cell, limiting the CAR-T cell's killing ability. CB-010 cells lack PD-1 on their surface and therefore are insensitive to PD-L1 expression. CB-010 cells are designed to maintain high antitumor activity for an extended duration.*

Target Indication

We are developing CB-010 for the treatment of r/r B-NHL. Non-Hodgkin lymphoma is the most common hematologic malignancy with an estimated 81,560 cases or 4% of all cancers diagnosed in the United States in 2021. B-NHL makes up 80 to 85% of those non-Hodgkin lymphoma cases.

B-NHL is a heterogeneous malignancy that is monoclonal in nature and arises in lymphocytes. The disease can often be traced to specific stages in lymphoid maturation. Most malignant lymphocytes derive from mature B cells or from lymphocytes of germinal center origin. The malignant cells have acquired the ability to proliferate, evade the host immune response, and avoid cellular apoptosis.

Overall, for aggressive r/r B-NHL, newer immunologically-mediated therapies under investigation include checkpoint inhibitors and CAR-T cells. FDA approved autologous CD19-specific CAR-T cell therapies have shown significant complete response rates, improved progression-free survival, and extended overall survival. Despite the clinical benefits of these approved autologous CAR-T cell therapies, they are expensive and challenging to manufacture, and many patients are ineligible, cannot wait the long vein-to-vein time, and may require bridging therapy. Thus, there remains significant unmet medical need in r/r B-NHL.

Clinical Development Plan

CB-010 is undergoing evaluation in our ANTLER phase 1 clinical trial for the treatment of adult patients with aggressive forms of r/r B-NHL. The patient population includes individuals for whom at least two lines of chemo- and/or immunotherapy have failed and who have not received CD19-targeted therapy previously. The patient population in the trial includes the following aggressive B-NHL subtypes: diffuse large B cell lymphoma ("DLBCL"); high grade B cell lymphoma ("HGBL"); transformed follicular lymphoma ("tFL"); primary mediastinal large B cell lymphoma ("PMBCL"); follicular lymphoma ("FL"); marginal zone lymphoma ("MZL"); and mantle cell lymphoma ("MCL").

Patients in our ANTLER phase 1 clinical trial receive a chemotherapy regimen prior to CAR-T cell infusion. The chemotherapy regimen includes two agents, cyclophosphamide and fludarabine, which are generally used for lymphodepletion prior to autologous CAR-T cell therapy. To ensure optimal engraftment of the allogeneic CB-010 cells, we use a more intensive regimen of these chemotherapeutic agents than has been previously used with allogeneic CAR-T cell therapies, namely cyclophosphamide at 60 mg/kg/day for 2 days, then fludarabine at 25 mg/m^2/day for 5 days. Our lymphodepletion regimen provides treatment flexibility so that the dosing may be modified to suit the patient's tolerance to the chemotherapy. We adapted our lymphodepletion protocol from one previously described by investigators at the National Institutes of Health, which was used in multiple clinical trials for autologous CAR-T cell therapies as well as other cellular therapies. The increased intensity refers to both the amount of each agent used and the timing of dosing. The objectives of the trial include the incidence of adverse events defined as dose-limiting toxicities after CB-010 infusion, the overall response rate, and the identification of the recommended phase 2 dose ("RP2D"), as shown in figure 12 below.

Our ANTLER phase 1 clinical trial is being conducted in two parts and we estimate enrolling up to approximately 50 patients across multiple centers in the United States. Part A is a dose escalation following a standard 3 + 3 design, with sequential, increasing single doses of CB-010. Part B is the expansion portion where patients will receive CB-010 at the dose determined in Part A. We expect to disclose initial clinical data from this trial at a medical conference in 2022.

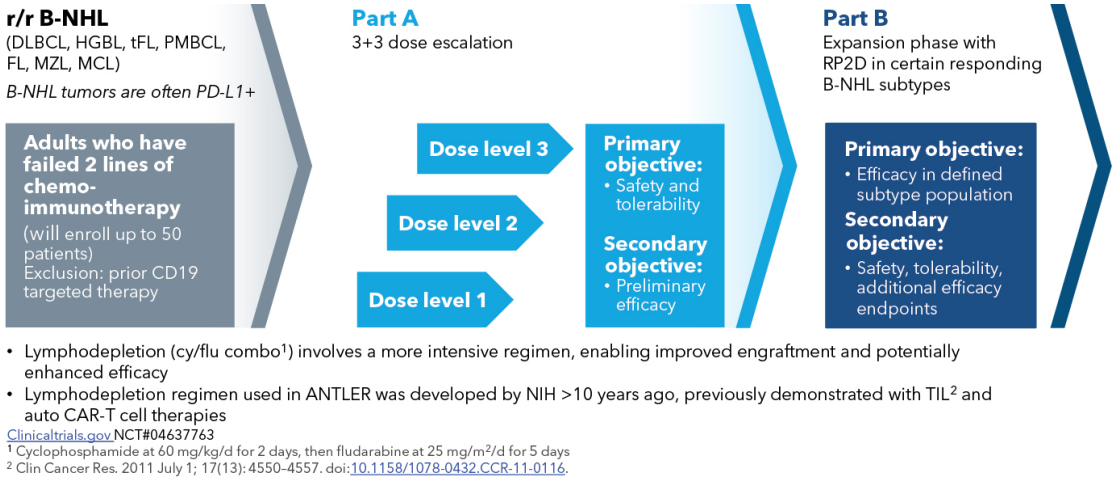


Figure 12. *Our ANTLER phase 1 clinical trial is designed to evaluate CB-010 in r/r B-NHL lymphoma patients. It is an open-label phase 1 trial expected to enroll up to approximately 50 participants in total. The study consists of two parts: Part A is a dose escalation with a 3 + 3 design, with sequential, increasing single doses. Part B is an expansion portion where patients will receive CB-010 at the RP2D, determined in Part A.*

Preclinical Data

In our preclinical studies, we demonstrated that the removal of the PD-1 checkpoint from the CB-010 CAR-T cells provided a statistically significant survival advantage in mice bearing robust and metastatic B cell tumors. To evaluate the impact of the PD-1 knockout on CB-010 CAR-T cell exhaustion and antitumor activity, we compared CB-010 CAR-T cells to conventional allogeneic CD19 CAR-T cells that express PD-1 in a long-term established tumor xenograft model. We engrafted immunodeficient mice in an orthotopic manner (by intravenous injection to ensure distribution within the bloodstream, lymphatics, and bone marrow) with the acute lymphocytic leukemia ("ALL") tumor model NALM-6 that expresses PD-L1. We allowed the tumors to engraft in the mice for

23 days to ensure that the tumors were metastatic to reflect the human condition with B-NHL. Once the tumors were well-established and metastatic, we treated the mice in three separate groups with the following different materials:

- Phosphate-buffered saline ("PBS"), a negative control;
- Conventional allogeneic CD19 CAR-T cells, T cells with the anti-CD19 CAR used in CB-010 inserted into the *TRAC* locus, but without the PD-1 knockout; and
- CB-010.

As shown in figure 13 below, all of the mice had robust tumor burden after 23 days of tumor engraftment as shown by imaging (color bar indicates more tumor growth, from blue to red). On day 0, each cohort of animals received a single dose of either PBS (negative control), the conventional allogeneic CD19 CAR-T cells, or CB-010 cells. By day 14 following dosing (D14 post CAR-T), animals that received PBS had become more metastatic, whereas both of the CD19-specific CAR-T cell therapies had eradicated the established tumors. Following initial tumor clearance, the animals treated with the conventional allogeneic CD19 CAR-T cell therapy experienced a rapid recurrence of their tumor. For example, by day 108 following dosing, half the mice treated with the conventional allogeneic CD19 CAR-T cell therapy had expired from their recurrent tumor burden, and the surviving mice in that cohort had metastatic disease. In contrast, by day 108 following dosing, all of the CB-010-treated mice were alive and few had detectable tumor burden. As shown in the survival curve in figure 13 below, all of the mice treated with the conventional allogeneic CD19 CAR-T cells had succumbed to their tumors by approximately day 135, while all but one of the CB-010 treated mice were still alive by day 160.

Overall, our data demonstrate that the removal of the PD-1 checkpoint from the CB-010 CAR-T cells provided a statistically significant survival advantage in mice bearing robust and metastatic B cell tumors. Our data suggest that the PD-1 knockout may have led to a more robust debulking of the tumor by CB-010 during the early part of the study compared to the conventional allogeneic CD19 CAR-T cells, leading to a reduction in the recurrence of the tumor cells. Based on these data, we believe CB-010 has the potential for a better therapeutic index compared to other allogeneic CAR-T cells. If a lower dose of CB-010 has meaningful activity in the clinical setting, it would lead to several potential advantages including limited toxicity, increased numbers of doses per manufacturing run, and a reduced cost of goods.

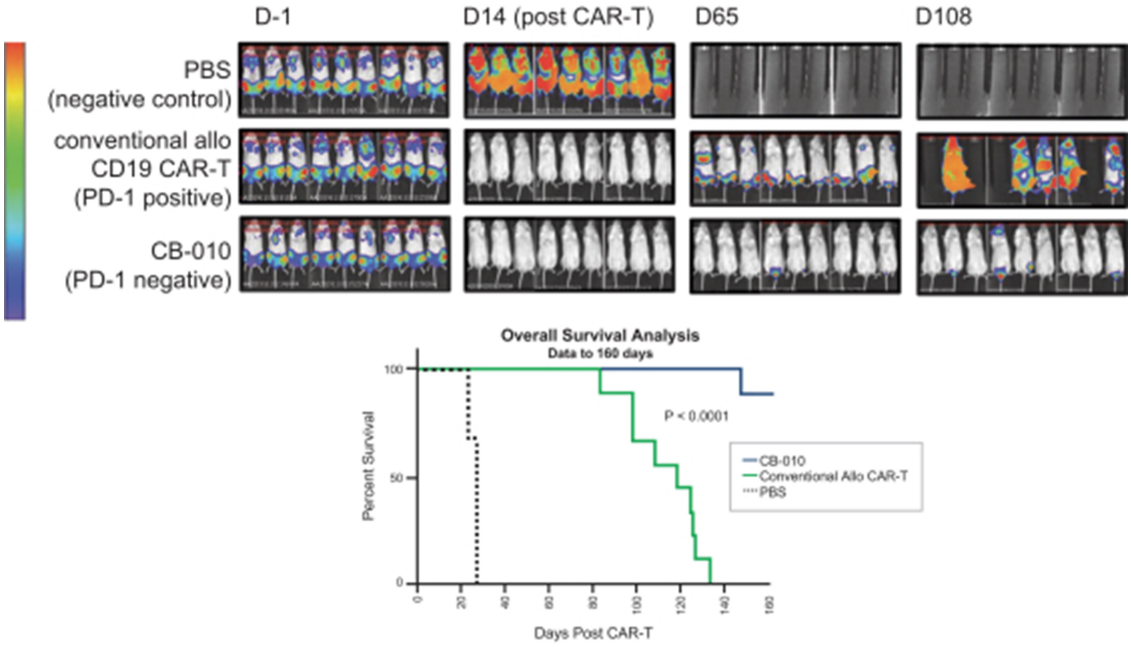


Figure 13. *Our preclinical mouse xenograft model demonstrates that CB-010 leads to a significant survival advantage over a conventional allogeneic CAR-T lacking a PD-1 knockout.*

In addition, as shown in figure 14 below, a single-dose CB-010 treatment led to robust, reproducible, and statistically significant survival in mice bearing DLBCL tumor cells, MCL tumor cells, or a patient-derived xenograft ("PDX") model of DLBCL.

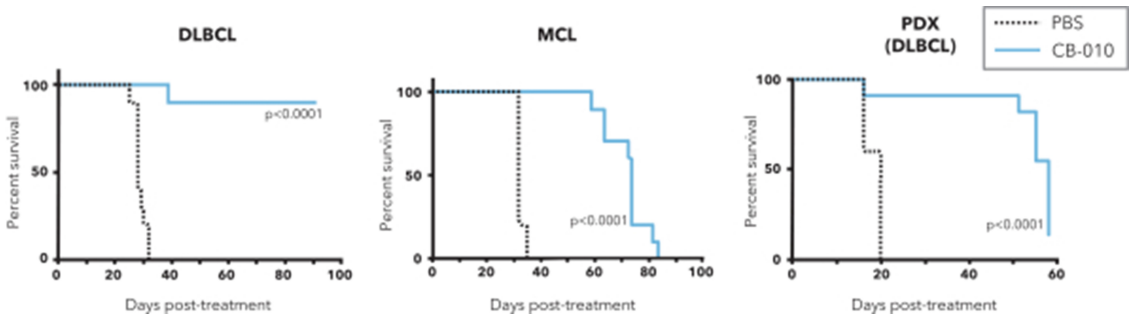


Figure 14. *CB-010 demonstrates statistically significant preclinical survival benefit across B-NHL indications.*

Together, our data support the efficacy of CB-010 in the treatment of CD19-positive B cell malignancies in mice. In addition, we determined in our *in vitro* studies that the knockout of PD-1 does not impair CAR-T cell activity. We characterized the antitumor activity of CB-010 CAR-T cells *in vitro* by co-incubating CB-010 cells with tumor cells of B cell origin. For example, CB-010 cytotoxic activity was tested *in vitro* against a CD19-positive model cell line of DLBCL (Toledo cells). As shown in figure 15 below, CB-010 cells demonstrate dose-dependent and robust cytotoxic activity at a range of effector-to-target ratios compared to negative control cells in which the *TRAC* gene was knocked out but no CAR was inserted, called *TRAC* KO, or compared to cells without any genome editing, called wild-type ("WT"). We additionally compared the cytotoxic activity of CAR-T cells where we inserted the CAR into the *TRAC* locus, but did not knock out PD-1, called conventional allogeneic CD19 CAR-T cells. CB-010 and conventional allogeneic CD19 CAR-T cells exhibit equivalent cytotoxic activity demonstrating that the PD-1 knockout does not impair cytotoxic activity.

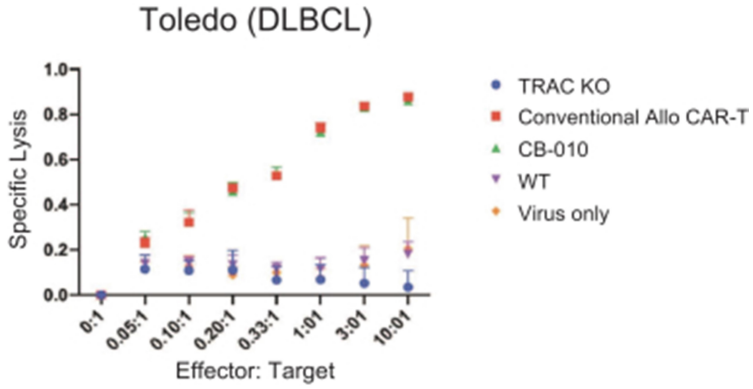


Figure 15. *Our in vitro studies demonstrate that the PD-1 knockout does not impair CAR-T cell activity.*

We evaluated the preclinical safety of CB-010 in mice and determined that CB-010 does not lead to GvHD in our mouse models. For comparison, we evaluated mice that received normal human T cells that were not genome edited and therefore express the TCR. In our study, we observed that the normal, unedited human T cells caused GvHD in the mice, as we expected, because the T cells could recognize the mouse tissues as foreign. GvHD was measured as changes in body weight and other clinical signs. Importantly, we observed that CB-010 did not induce any signs of GvHD. These observations were part of the data package that we provided to the FDA for our IND application.

CB-011

Overview: Strategy and Rationale

CB-011 is an allogeneic CAR-T cell therapy targeting BCMA-positive malignancies. The CB-011 cells express our proprietary, potent, humanized anti-BCMA CAR that exhibits better performance in preclinical *in vivo* antitumor activity assays

compared to other anti-BCMA CARs we evaluated. We acquired a novel humanized scFv directed to BCMA that we use for the generation of the BCMA-specific CAR in CB-011.

We believe that the edits we make to immune cloak the product will maintain the CB-011 cells in the patient's circulation longer. CB-011 is a preclinical product candidate and we make a total of four genome edits using the Cas12a chRDNA technology to manufacture CB-011.

- *TRAC knockout:* We knock out the *TRAC* gene to eliminate expression of the TCR from the surface of the CAR-T cells. The removal of TCR expression is intended to prevent GvHD in patients.

- *Site-specific insertion of the anti-BCMA CAR:* We insert the BCMA-targeted CAR into the *TRAC* gene by AAV6 transduction and homology directed repair. We believe site-specific insertion of the CAR has advantages compared to random integration mediated by lentiviral or retroviral insertion. For example, random integration leads to the risk of unintended gene disruption which is avoided via site-specific insertion. The insertion of the CAR yields a cell product that exhibits BCMA-specific cytotoxicity.

- *B2M knockout:* We knock out B2M, a protein necessary for the presentation of HLA class I molecules on the surface of a T cell. The disruption of the B2M locus yields a cell product that does not express endogenous HLA class I molecules, limiting the ability of the patient's T cells to detect and reject the CAR-T cell therapy.

- *Site-specific insertion of a B2M–HLA-E fusion protein:* We site-specifically insert a transgene that fuses B2M, HLA-E, and a peptide by AAV6 transduction and homology directed repair. HLA-E is a minor class I antigen that interacts with NK cells. This insertion, combined with the B2M knockout, yields a cell product that has only HLA-E, and no other class I antigens, on its surface. The presence of only HLA-E is designed to prevent both the patient's T cells and NK cells from rapidly rejecting the therapy.

In figure 16 below, we outline the impact of the different edits in the CB-011 product candidate to demonstrate how different leukocyte immune cells of the patient will interact with the CAR-T cells.

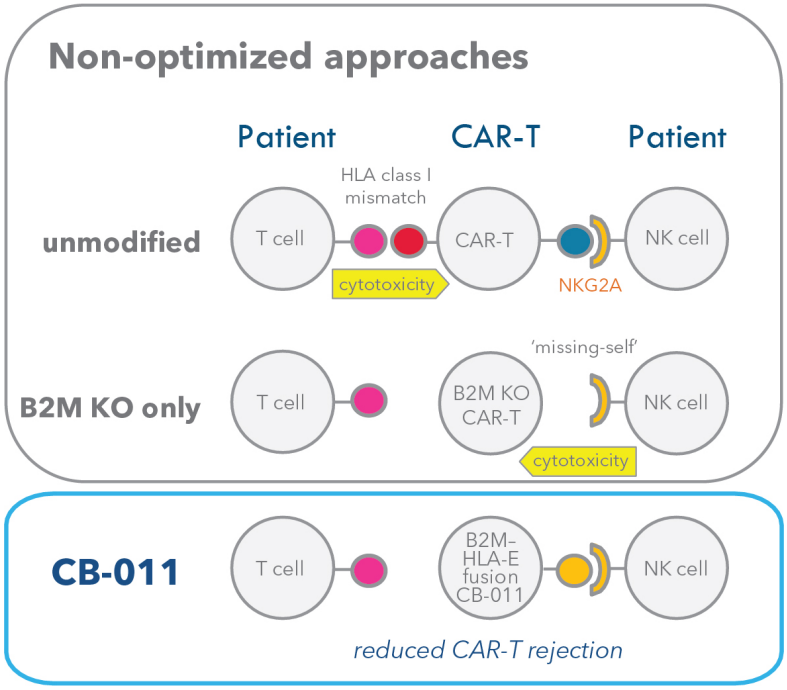


Figure 16. *Our CB-011 cloaking strategy blunts immune-mediated rejection by patient T and NK cells.*

In this example, we show that unmodified CAR-T cells, those that have intact HLA class I antigens, are subject to rejection by the patient's cytotoxic T cells once the T cells recognize the allogeneic CAR-T cells as foreign. This is mediated by the presentation of peptides by the CAR-T cells via their HLA class I antigens to the patient's immune system that will recognize them as

foreign since the CAR-T cells are derived from a non-familial healthy donor. If we only knock out the *B2M* gene, thereby eliminating all HLA class I antigens, the cytotoxic T cells of the patient would no longer recognize the CAR-T cells as foreign. However, the NK cells of the patient would detect the lack of HLA class I antigens, a concept known as "missing self," which would unleash the activity of the NK cells, enabling them to destroy the allogeneic CAR-T cells. In CB-011, we protect the CB-011 CAR-T cells from rejection by both the patient's cytotoxic T cells and NK cells by removing endogenous HLA class I antigen presentation through the knockout of *B2M* and by inserting a B2M–HLA-E fusion into the *B2M* locus. We believe that this strategy will enable the CB-011 CAR-T cells to remain in circulation longer in patients, providing for increased potential of antitumor activity.

Target Indication

We are developing CB-011 for the treatment of r/r MM. In 2021, 18% of hematologic malignancies in the United States and 1.8% of all cancers were MM. The median age of diagnosis is 69 years, and there are an estimated 32,270 new cases in the United States with an estimated 12,830 deaths each year. Five-year survival in these patients is approximately 47%.

There has been significant interest in and activity against BCMA as a target over the past two years with the approval of an antibody drug conjugate therapy and two new CAR-T cell therapy products targeting BCMA. FDA-approved autologous BCMA CAR-T cell therapies have shown significant complete response rates, improved progression-free survival, and extended overall survival. Despite the clinical benefits of these approved autologous CAR-T cell therapies, they are expensive and challenging to manufacture, and many patients are ineligible.

Additionally, many treatments for MM are multidrug regimens comprising varying routes of administration and/or convoluted dosing schedules; these regimens can be complex and burdensome for both patients and physicians. The need for simplified dosing schedules remains. Thus, although we expect that approvals of additional therapies may serve to partially mitigate the need for more treatment options in r/r MM, therapies that prolong the lives of r/r MM patients or delay disease progression, address simpler manufacturing, and streamline dosing schedules are critical to address the unmet medical need in r/r MM.

Clinical Development Plan

We expect to submit an IND application in 2022 for a phase 1 clinical trial to evaluate CB-011 in patients with r/r MM. We anticipate evaluating CB-011 in patients with a documented diagnosis of active MM according to International Myeloma Working Group diagnostic criteria who have received at least three prior lines of therapy with previous exposure to a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody (unless intolerant to these therapies) and have progressive disease within 12 months of the last treatment or are refractory to the last line of therapy.

Preclinical Data

To demonstrate that the B2M–HLA-E fusion protects CB-011 from NK-mediated cell killing, we set up an *in vitro* study where NK cells were incubated with CAR-T cells containing the attributes of the three examples described in figure 16 above. The results of this analysis are shown in figure 17 below. The unmodified CAR-T cells were subject to killing, or lysis, by the NK cells. The knockout of *B2M* led to enhanced killing by the NK cells, demonstrating the "missing self" hypothesis. Insertion of the B2M–HLA-E fusion in the CB-011 cells protected them from NK cells more than the unmodified cells, indicating they could resist killing by NK cells, thereby suggesting longer circulation potential in patients.

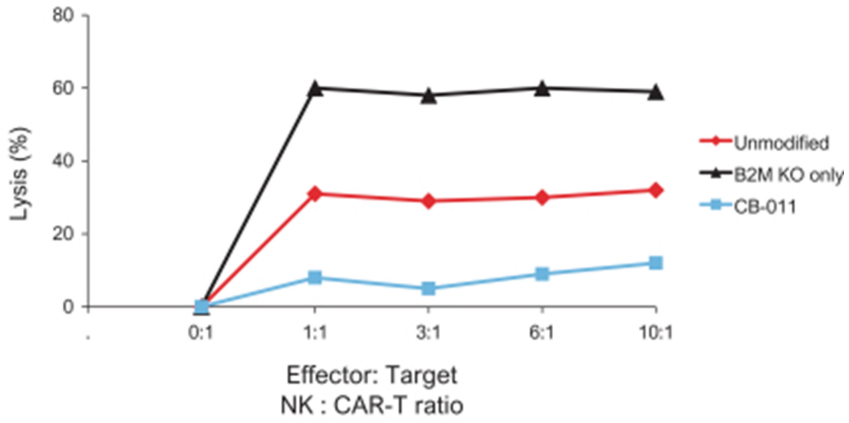


Figure 17. *Our in vitro data demonstrate that the B2M–HLA-E fusion protects CB-011 CAR-T cells from NK cell-mediated lysis. We measured in vitro cytotoxicity 24 hours after CAR-T cell co-incubation with NK-92 cells.*

We acquired a novel humanized scFv directed to BCMA that we use for the generation of the CB-011 CAR based on preclinical *in vivo* antitumor activity that exhibited better performance compared to other BCMA-specific scFvs we evaluated. For example, we constructed CARs using this and other scFvs, and we evaluated the antitumor potential of CAR-T cells expressing these different CARs in mice bearing BCMA-positive tumors. In figure 18 below, we show two examples of mouse xenograft data comparing CB-011 cells with CAR-T cells expressing an alternative BCMA CAR previously described in the literature and evaluated in multiple clinical trials. CB-011 cells led to statistically significantly longer survival of the tumor-bearing mice. The studies were conducted in two different tumor xenograft models, including MM (left panel) and a BCMA+ tumor xenograft (right panel).

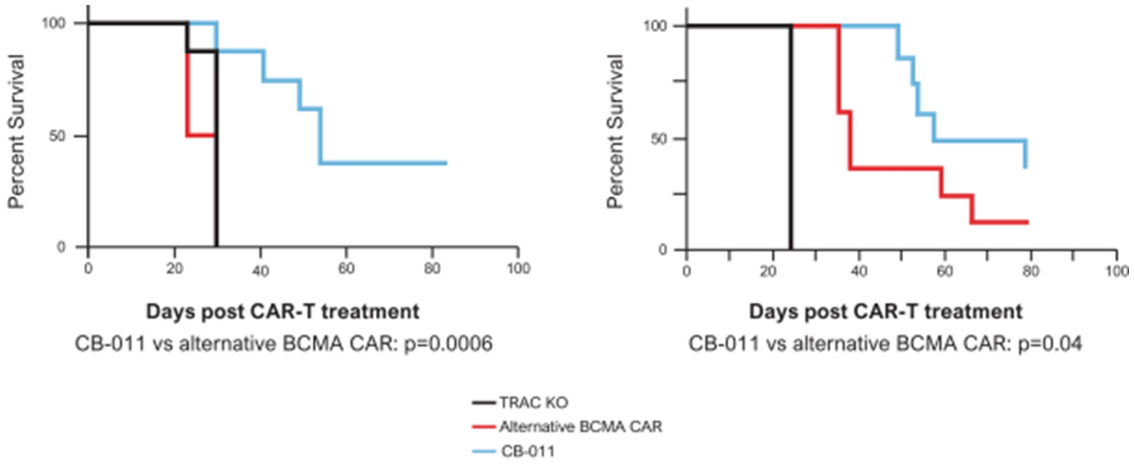


Figure 18. *CB-011 led to statistically significant and longer survival of tumor-bearing mice relative to alternative anti-BCMA CAR-T cells. Left panel represents established subcutaneous multiple myeloma tumor xenografts after a single dose CAR-T cell treatment. Right panel represents established orthotopic BCMA+ tumor xenografts after a single dose CAR-T cell treatment. TRAC KO cells, a negative control, are T cells with only a knockout of the TRAC gene and no CAR.*

We evaluated the safety of CB-011 in a mouse model of GvHD. The maximum number of injectable CB-011 cells (3 x 10^7/mouse) was used to determine if CB-011 induced GvHD in the mice, compared to 3 x 10^7 WT T cells and vehicle (phosphate-buffered saline) negative control. In figure 19 below, we show that only the WT T cells induced clinical signs of GvHD, including loss of body weight, changes in fur texture, and death, whereas CB-011 did not induce any signs of GvHD.

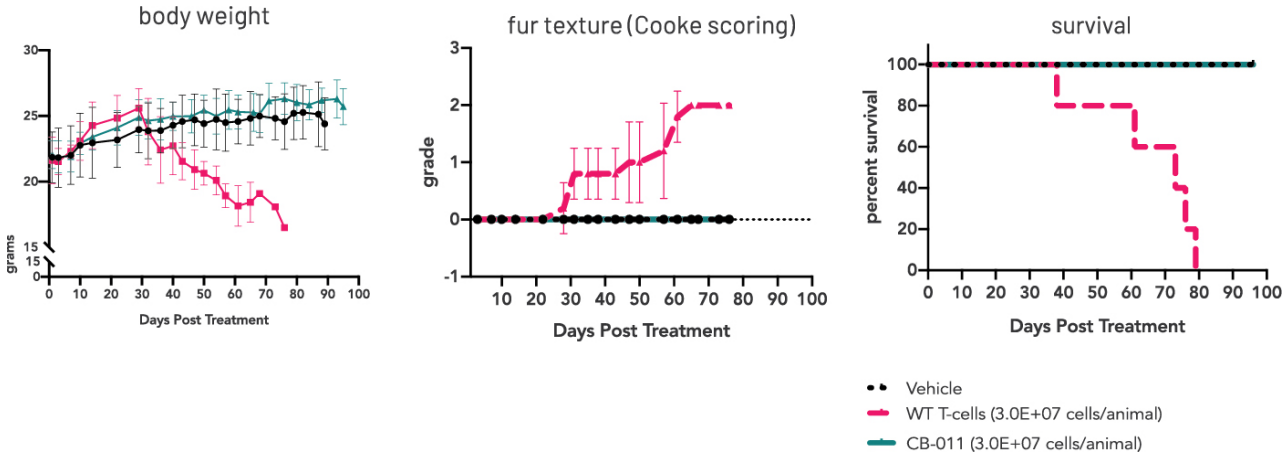


Figure 19. *CB-011 does not induce GvHD in a mouse model. Left panel represents body weight, middle panel fur texture based on Cooke scoring, and right panel represents mouse survival. Only WT T cells induced signs of GvHD.*

CB-012

Overview: Strategy and Rationale

CB-012 is our allogeneic CAR-T cell product candidate that targets the antigen CD371, also known as CLL-1 or CLEC12A, a receptor expressed on AML tumor cells. Our goal is to make multiple edits to this product candidate using our Cas12a chRDNA technology to enhance its antitumor activity. We believe CD371 is a compelling target for the treatment of AML. An important aspect of the CD371 antigen is its expression on >90% of AML tumors and leukemic stem cells and its lack of expression on hematopoietic stem cells ("HSCs"). The absence of expression on HSCs indicates that these bone marrow cells will not be targeted by the CD371-directed CB-012 CAR-T cells, thereby preventing a patient from loss of a critical compartment of their immune system vital for fighting infections and cancer. As such, patients receiving CB-012 treatment would not require an HSC transplant to provide them with myeloid compartment cells for sustained immunity.

We have in-licensed from Memorial Sloan Kettering Cancer Center ("MSKCC") a panel of fully human scFvs targeting CD371 from which we will select the appropriate scFv for the generation of our CAR. As described above for CB-010 and CB-011, an important aspect of CB-012 will be appropriately armoring the CAR-T cells using our Cas12a chRDNA technology to improve the persistence of antitumor activity. We are evaluating several options including the PD-1 knockout and immune-cloaking approaches. We are considering additional armoring technologies which may include editing that will help the CAR-T cells survive longer, withstand functional suppression by the tumor cells, and enhance their antitumor activity.

Target Indication

Acute myeloid leukemia is a cancer of the bone marrow currently treated with chemotherapy, radiation, targeted therapies, and/or HSC transplant. In 2021, there were approximately 20,000 new cases of AML in the US, with >40,000 new patients in the seven major global markets. Five-year survival in these patients is <30%.

Intensive induction chemotherapy, known as 7 + 3, consisting of cytarabine and an anthracycline is the most effective therapy for adults newly diagnosed with AML, although the treatment has significant associated toxicities. Thus, there remains significant unmet need in the treatment of AML.

Clinical Development Plan

We expect to submit an IND application for CB-012 in 2023 with the intent to evaluate this therapy in patients with r/r AML in a phase 1 clinical trial.

Preclinical Data

We evaluated one of the CD371-specific scFvs that we in-licensed in a CAR that we expressed on T cells. The CD371-specific CAR-T cells were tested in an established mouse xenograft model of AML. For comparison, we evaluated two negative controls, vehicle (PBS) and human T cells with only a *TRAC* KO and no CAR. As shown in figure 20 below, the CD371-specific

CAR-T cells significantly extended survival in the AML tumor-bearing mice compared to mice that received either of the two negative control treatments. We plan to use genome edits to armor CB-012 for enhanced persistence and greater antitumor activity.

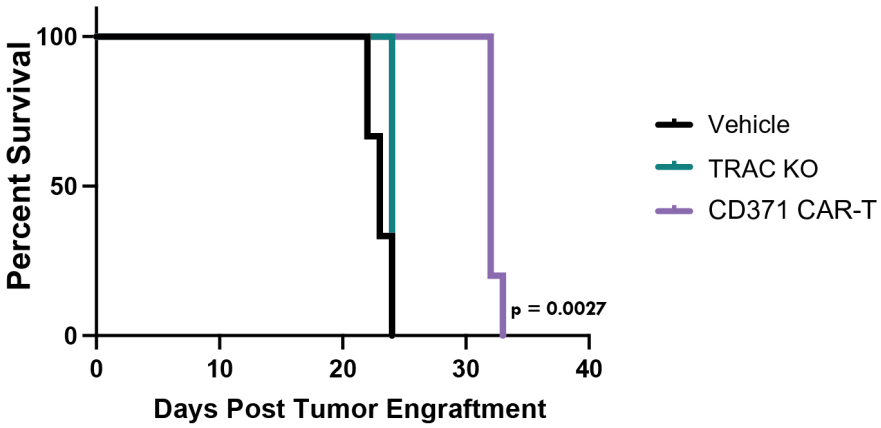


Figure 20. *We conducted a mouse tumor xenograft study evaluating CD371-specific CAR-T cells. Our work demonstrated that CD371-specific CAR-T cells confer longer-term survival in a xenograft model of AML compared to control treatments.*

CB-020

Overview: Strategy and Rationale

Our CB-020 program is a CAR-NK cell product candidate derived from edited iPSCs designed to target an antigen expressed on solid tumors and associated metastases. Despite their clinical success against hematologic malignancies, CAR-T cells have not yet demonstrated broad, robust antitumor activity in the solid tumor setting. NK cells are a compelling platform for cell therapy development for targeting multiple different solid tumors. NK cells inherently have antitumor activity against primary solid tumors and metastases and they are naturally transferable between donor and patient. We believe they are a promising cell type for new therapeutic development. In order to perform multiple, sophisticated genome edits to empower NK cells with the attributes we believe will be necessary to successfully target the intended solid tumor and overcome the immunosuppressive tumor microenvironment, we have developed a proprietary protocol to edit iPSCs and differentiate them into iNKs. See figure 21 below.

There are multiple advantages of using iPSCs. They are amenable to higher numbers of genome-editing events than most primary cells. A solitary clone isolated after genome editing will have all the intended edits. This is distinct from the allogeneic CAR-T cell products derived from healthy donor leukapheresis where a proportion, but not all, of the T cells in a batch contain all the intended edits. This fully edited iPSC will then be differentiated into iNK cells and expanded for therapeutic use. This platform will enable us to generate sophisticated, armored iNK cell product candidates with attributes necessary for targeting solid tumors.

An outline of the multi-step iPSC to iNK platform we developed to generate CB-020, and future product candidates, is shown in figure 21 below.

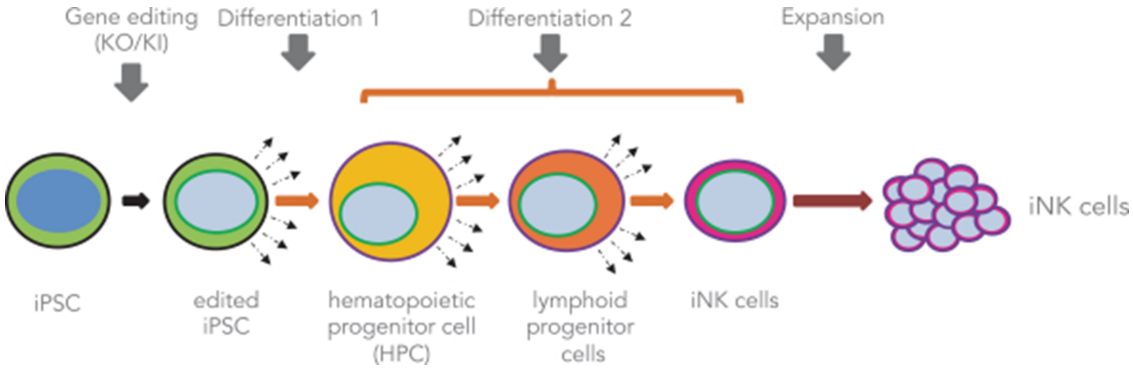


Figure 21. *Our platform for editing iPSCs and differentiating them into iNKs.*

Target Indication

Multiple clinical trials are evaluating autologous CAR-T and CAR-NK cell therapies targeting solid tumors. Although some activity has been observed clinically, the overall response rates with these therapeutic modalities have been significantly lower and fewer complete responses have been observed compared to those observed when treating hematologic malignancies. Some of the challenges facing these therapies may be that the CAR-T and CAR-NK cells have difficulty in trafficking to the tumor, surviving and proliferating at the tumor site, infiltrating the tumor, surviving the immunosuppressive tumor microenvironment, and debulking a heterogeneous tumor that may not uniformly express the target of the CAR-T or CAR-NK cell. Overall, a significant unmet need remains in the treatment of solid tumors.

Preclinical Data

In figure 22 below, we demonstrate that iNK cells differentiated from iPSCs express a key defining antigen called CD56, or NCAM, that is indicative of the NK cell lineage. Additionally, we show that the iNK cells exhibit the expected polyfunctionality of NK cells. For example, we show that the iNK cells exhibit dose-dependent cytotoxic activity and interferon gamma ("IFNg") secretion when co-incubated with tumor cells *in vitro*. Further, when the iNK cells are co-incubated *in vitro* with CD20-positive tumor cells and rituximab, an anti-CD20 antibody, we observe antibody-dependent cell cytotoxicity ("ADCC").

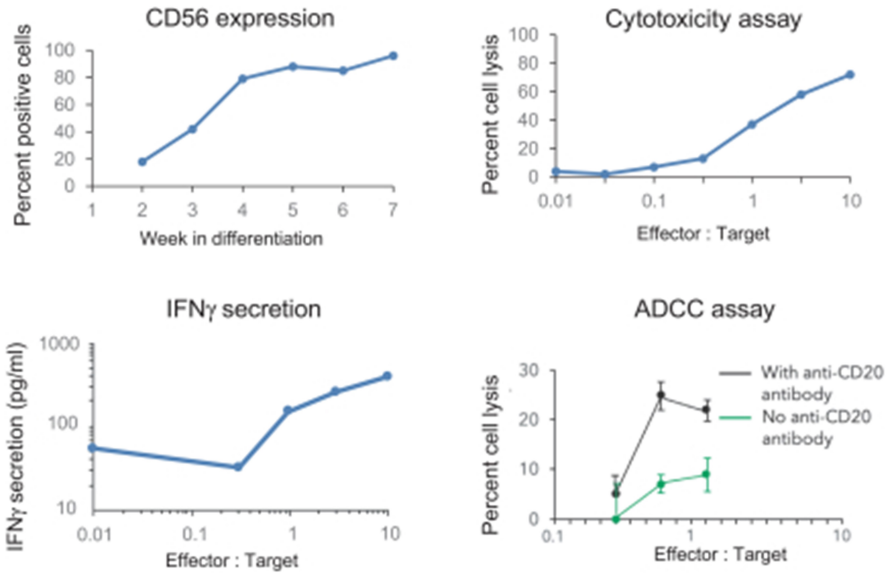


Figure 22. *iNK cells differentiated from iPSCs using our differentiation protocol demonstrate the expected polyfunctionality of NK cells.*

We evaluated iNKs that were generated from our differentiation and expansion protocols in an orthotopic established xenograft model of ovarian cancer. For comparison, we evaluated primary human NK cells derived from a fresh blood sample, and a vehicle negative control (PBS). As shown in figure 23 below, the iPSC-derived iNK cells significantly extended survival in the ovarian tumor-bearing mice similar to the activity of the blood-derived NK cells, both compared to mice that received the negative

control treatment. These data demonstrate that iNKs generated from our differentiation protocols exhibit antitumor activity, which we plan to enhance in CB-020 via genome edits such as the addition of a CAR and one or more armoring strategies.

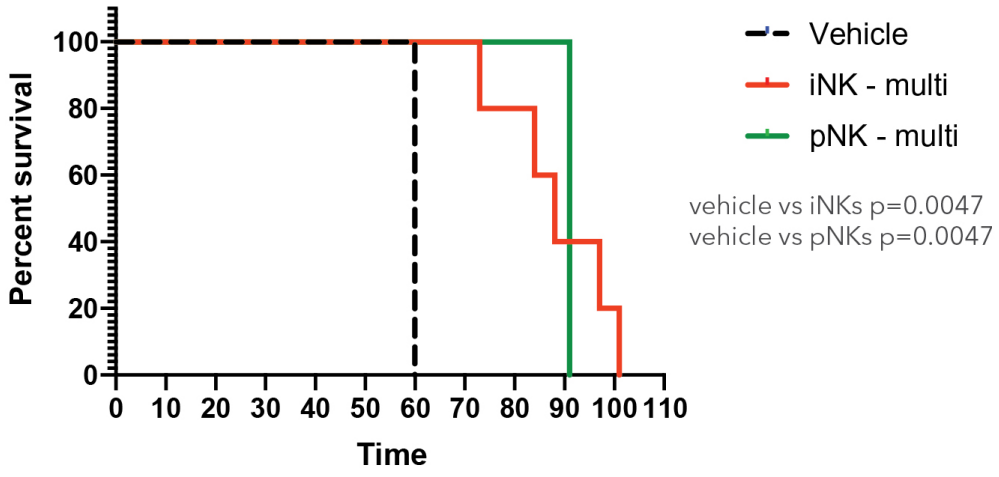


Figure 23. *We conducted a mouse tumor xenograft study evaluating our iNK cells derived from iPSCs using our differentiation and expansion protocols. Our work demonstrated that iNKs confer longer-term survival in a xenograft model of ovarian cancer.*

For CB-020, we plan to implement multiple genome edits that we believe will address some or all of the challenges described above including solid tumor heterogeneity, immunosuppression, trafficking, and tumor infiltration, as well as other strategies to maintain persistence such as those described for our CAR-T cell product candidates. A clonal genome-edited iPSC line will be isolated, evaluated for genomic integrity, differentiated into iNK cells, expanded in culture using our established process, and evaluated in preclinical models of safety and efficacy prior to IND filing. We expect to announce target selection for our CB-020 product candidate in 2022. Additionally, we plan to disclose multiple types of armoring strategies that could be useful in this product candidate or for future CAR-NK cell therapies.

Our iNK platform provides the potential for multiple future cell therapeutics beyond CB-020, targeting different solid tumor antigens and types. The biology of a given tumor will help define the nature of the genome edits we implement to customize each product to address the challenges of one or more particular malignancies. We are evaluating multiple targets and strategies for the development of this product series.

AbbVie Collaboration Product Candidates

Under the AbbVie Agreement, for each of AbbVie's two program slots, we are collaborating to identify and develop one or more collaboration allogeneic CAR-T cell therapies for AbbVie directed toward the single cancer target or target combination chosen by AbbVie and as described in an applicable research plan, utilizing our Cas12a chRDNA genome-editing and cell therapy technologies.

AbbVie has selected its initial targets and has reserved six additional targets, which may be used or substituted into the two program slots or used for the third or fourth program slots if AbbVie expands the number of program slots during the collaboration. We are conducting preclinical research, development, and manufacturing activities on AbbVie's allogeneic CAR-T cell product candidates.

Strategic Agreements

We recognize the broad opportunity presented by our genome-editing technologies to benefit patients, and we appreciate that one company is unlikely to have sufficient resources to fully exploit this potential across multiple indications and applications. As part of our strategy to maximize the value and benefit of our technologies, we have entered into a strategic collaboration with AbbVie and intend to explore mutually beneficial strategic collaborations with other biotechnology or pharmaceutical companies in the future. Additionally, we have in-licensed or taken assignment of key technologies important for the development of our product candidates

AbbVie Manufacturing Management Unlimited Company

On February 9, 2021, we entered into the AbbVie Agreement. Pursuant to the AbbVie Agreement, AbbVie selects one target or, for a dual CAR-T product candidate, two targets (each, a "Program Slot") to develop collaboration CAR-T product candidates (and corresponding licensed products). For each of AbbVie's two Program Slots (or up to four Program Slots, if AbbVie elects to expand the number as discussed below), we will collaborate to develop one or more collaboration allogeneic CAR-T products directed toward the single cancer target or target combination chosen by AbbVie and as described in an applicable research plan, utilizing our Cas12a chRDNA genome-editing and cell therapy technologies. We granted AbbVie an exclusive, royalty-bearing, worldwide license, with the right to grant sublicenses, under our Cas12a chRDNA and cell therapy intellectual property, as well as certain genome-editing technology that we may acquire in the future, and intellectual property that may be developed under the collaboration, solely for AbbVie to develop, commercialize, manufacture, and otherwise exploit the collaboration CAR-T product candidates in the field of human diagnostics, prophylactics and therapeutics. Under the terms of the AbbVie Agreement, we will conduct certain preclinical research, development, and manufacturing activities under the collaboration, including certain activities for the manufacture and supply of licensed product for AbbVie's phase 1 clinical trials. AbbVie will reimburse us for all such activities, including reimbursement for time spent by employees at a designated FTE rate. The duration of the collaboration is not fixed. We have formed a joint governance committee ("JGC") to manage the collaboration.

We received $30.0 million in an upfront cash payment and $10.0 million in an equity investment from AbbVie. During the collaboration, AbbVie may expand from two Program Slots to a total of four Program Slots by paying us an additional $15.0 million for each Program Slot, provided that AbbVie must make the payment within the earlier of (i) 60 calendar days following completion of the phase 1 clinical studies for the initial collaboration CAR-T and (ii) December 31, 2025. Under the terms of the AbbVie Agreement, we are eligible to receive up to $150.0 million in future developmental, regulatory, and commercialization milestones for each Program Slot and up to $200.0 million in sales-based milestones for each Program Slot. We are also eligible to receive global royalties on incremental net sales of licensed products sold by AbbVie, its affiliates, and sublicensees in the high-single-digit to low-teens percent range, subject, in certain instances, to various reductions.

AbbVie has selected initial targets and has reserved six additional targets, which may be used or substituted into the two Program Slots or used for the third or fourth Program Slots if AbbVie expands the number of Program Slots during the collaboration. We have identified four unavailable targets that AbbVie cannot pursue as long as we meet certain criteria. Additionally, except for AbbVie's reserved targets and our unavailable targets, if AbbVie wishes to propose a different target, there is a gatekeeper mechanism whereby such target may or may not be available to AbbVie.

The term of the AbbVie Agreement will continue in force and effect until the date of expiration of the last royalty term of the last country in which a licensed product is exploited. On a licensed product-by-licensed product and country-by-country basis, the royalty term is the period of time beginning on the first commercial sale of a licensed product in a country and ending on the latest of the following three dates: (i) the expiration, invalidation, revocation, cancellation, or abandonment date of the last Caribou patent that includes a valid claim that claims either (A) the collaboration CAR-T product in the licensed product, or (B) the method of making the collaboration CAR-T product in such licensed product in such country (in the case of (B), only for so long as no biosimilar product is commercially available in such country), in such country; (ii) 10 years from the first commercial sale of such licensed product in such country; and (iii) the expiration date of regulatory exclusivity for such licensed product in such country. The AbbVie Agreement may be terminated during the term by either party for an uncured material breach or bankruptcy. Additionally, AbbVie may terminate the AbbVie Agreement, in its entirety or on a licensed product-by-licensed product basis, effective immediately upon written notice to us, if AbbVie in good faith believes that it is not advisable for AbbVie to continue to exploit the collaboration on CAR-T products or licensed products as a result of a perceived serious safety issue. AbbVie may also terminate the AbbVie Agreement in its entirety, or, for any or no reason, upon 90 calendar days' prior written notice to us.

AbbVie does not have any rights to our CB-010, CB-011, CB-012, or CB-020 product candidates or any other product candidates that we may develop alone or with a third party in the future.

Memorial Sloan Kettering Cancer Center

On November 13, 2020, we entered into an Exclusive License Agreement with MSKCC (the "MSKCC Agreement"), under which we exclusively licensed from MSKCC know-how, biological materials, and related patent families to fully human scFvs targeting CD371 for use in T cells, NK cells, and genome-edited iPSCs for allogeneic CD371-targeted cell therapy (currently our CB-012 product candidate). We paid an upfront payment of cash and shares of our common stock and will owe annual license maintenance fees until we have commercial sales. For each licensed product, we will owe potential clinical, regulatory, and commercial milestone payments totaling up to $112.0 million and, if we, or our affiliates or sublicensees, receive regulatory approval for CB-012, we will owe low- to mid-single-digit percent royalties on net sales by us, our affiliates, and our sublicensees. Our license includes the right to sublicense through multiple tiers and we will owe MSKCC a percentage of upfront cash or equity received from our sublicensees. The percentage owed decreases as our product candidates move through development, starting at a low-double-digit percentage if clinical trials have not yet begun and decreasing to a mid-single-digit percentage if the product candidate is in later clinical trial stages. We are also responsible for a percentage of licensed patent costs. The MSKCC Agreement includes certain diligence milestones that we must meet; provided, however, that these may be extended upon payment of additional fees.

MSKCC is entitled to certain success payments if our stock value increases by certain multiples. The potential payments are based on multiples of the fair market value of our common stock compared with a split-adjusted initial share price of $5.1914 per share, as subject to future adjustments for stock splits, during a specified time period described below. Our common stock price will be determined by reference to the 45-day volume weighted-average trading price of our common stock. At our option, payments may be made in cash or common stock. The relevant time period commences when the first patient is dosed with our CB-012 product candidate in the first phase 1 clinical trial and ends upon the earlier of the third anniversary of approval of our biologics license application ("BLA") by the U.S. Food and Drug Administration ("FDA") or 10 years from the date the first patient was dosed with CB-012 in the first phase 1 clinical trial. Under the terms of the MSKCC Agreement, the aggregate success payments will not exceed $35.0 million. Additionally, if we undergo a change of control during the relevant time period, a change of control payment may be owed, depending upon the increase in our stock price due to the change of control and also to what extent success payments have already been paid. In no event will the combination of success payments and any change of control payment exceed $35.0 million. The relevant time period during which MSKCC is eligible for success payments and a change of control payment has not yet commenced.

We may terminate the MSKCC Agreement upon 90 calendar days' prior written notice to MSKCC. MSKCC may terminate the agreement in the event of our uncured material breach, bankruptcy, or criminal activity. If MSKCC materially breaches the MSKCC Agreement in certain circumstances (for example, granting a third party a license in our field), then during the time of such uncured material breach, MSKCC will not be entitled to receive any success payments or any change of control payment.

ProMab Biotechnologies, Inc. ("ProMab")

On January 31, 2020, we entered into a Sale and Assignment Agreement with ProMab (as amended, the "ProMab Agreement") under which we purchased a humanized scFv targeting BCMA and a patent family related thereto for an upfront cash payment of $0.4 million and the potential for future royalties. To date, three U.S. patents have granted (U.S. Patent Nos. 10,927,182; 11,021,542; and 11,142,583). Our anti-BCMA CB-011 product candidate, which is currently in preclinical studies, contains this BCMA scFv. Under the terms of the ProMab Agreement, in the event we, or our affiliates or licensees, receive regulatory approval for CB-011, we will owe ProMab low-single-digit percent royalties on net sales by us, our affiliates, and licensees until the expiration, abandonment, or invalidation of the last patent within the assigned patent family (i.e., 2040, without patent term adjustment ("PTA") or patent term extension ("PTE")). Such royalties may be reduced by no more than 50% if we must pay royalties to a third party for other intellectual property covering our product. Either party may terminate the ProMab Agreement in the event of an uncured material breach or bankruptcy of the other party. If ProMab terminates the ProMab Agreement due to our uncured material breach or bankruptcy, we must cease the manufacture, use, and sale of any products or product candidates incorporating the purchased anti-BCMA scFv.

Pioneer Hi-Bred International, Inc. ("Pioneer," now Corteva Agriscience)

On July 13, 2015, we entered into an Amended and Restated Collaboration and License Agreement (as amended, the "Pioneer Agreement") with Pioneer (then a DuPont company) that superseded and replaced a prior Collaboration and License Agreement entered into on September 10, 2014. Under the terms of the Pioneer Agreement, we and Pioneer cross-licensed background CRISPR intellectual property portfolios. Pioneer granted us an exclusive worldwide license, with the right to sublicense, to its background CRISPR intellectual property in the field of research tools, and a non-exclusive license, with the right to sublicense, for CRISPR in therapeutics and all fields outside of the Pioneer field, including in the field of human and animal therapeutics. We granted Pioneer an exclusive license, with the right to sublicense, to our background CRISPR intellectual property, including the CVC IP discussed below, in certain agricultural crops, specified microorganisms, a defined industrial bio field, and certain nutrition and health applications (the "Pioneer Exclusive Field"), and a non-exclusive license, with the right to sublicense, to Pioneer for CRISPR in certain defined fields outside of research reagents. The Pioneer Agreement continues until the expiration, abandonment, or invalidation of the last patent or patent application within the licensed intellectual property; provided, however, that the parties may terminate the Pioneer Agreement by mutual consent or either party may unilaterally terminate the Pioneer Agreement if there is an uncured breach of a payment obligation, bankruptcy, or failure to maintain or own licensed intellectual property by the other party if the non-breaching party is materially adversely affected by such failure. Under the terms of the Pioneer Agreement, we are obligated to pay low-single-digit percent royalties to Pioneer for our research tool products as well as certain sublicensing revenue in that field. We are eligible to receive milestone payments from Pioneer in the event certain regulatory and commercial milestones are met, for a total of up to $22.4 million, related to specified row crops and we are also eligible to receive low-single-digit percent royalties for defined agricultural products and certain sublicensing revenue in that field.

The chRDNA patent family was developed under a three-year research collaboration between us and Pioneer, which ended December 31, 2016. Initially, this patent family was owned by Pioneer under the terms of the Pioneer Agreement, and we and Pioneer split the costs of patent prosecution and maintenance equally. Pioneer granted us an exclusive license to the chRDNA patent family in the fields of human and animal therapeutics and research tools as well as a non-exclusive license in certain other fields outside of the Pioneer Exclusive Field. Through an amendment to the Pioneer Agreement, dated December 18, 2020, Pioneer assigned the chRDNA patent family to us. Pioneer retained all of its existing rights (including its sublicensing rights) to the chRDNA patent family despite the change in ownership. As consideration for the assignment, we made an upfront payment of $0.5 million and are obligated to pay all patent prosecution and maintenance costs going forward; up to $2.8 million in regulatory milestones for therapeutic products developed by us, our affiliates, and licensees; up to $20.0 million in sales milestones over a total of four therapeutics products sold by us, our affiliates, and licensees; and a percentage of sublicensing revenues received by us for licensing the chRDNA patent family. The sublicensing agreements that we entered into prior to December 18, 2020 (for example, the Intellia Agreement discussed below) are not subject to these economics; however, this amendment is applicable to the AbbVie Agreement.

Intellia Therapeutics, Inc. ("Intellia")

On July 16, 2014, we entered into a License Agreement (as amended, the "Intellia Agreement") with Intellia, LLC (now Intellia Therapeutics, Inc.), under which we granted Intellia an exclusive worldwide license, with the right to sublicense, to certain CRISPR-Cas9 technology for a defined field of human therapeutics in exchange for Intellia stock. The Intellia Agreement included a license to certain of our future CRISPR-Cas9 intellectual property until such time as our direct or indirect ownership percentage in Intellia dropped below 10%, called the IP cut-off date, which occurred on January 30, 2018. Intellia granted us an exclusive worldwide license, with the right to sublicense, to its CRISPR-Cas9 technology for all fields outside of the defined field of human therapeutics, including a license to certain of Intellia's future CRISPR-Cas9 intellectual property until the IP cut-off date. Each party had the right to opt in to any licenses in its field of use entered into by the other party prior to the IP cut-off date, subject to the terms and conditions of such license, and Intellia opted into our Pioneer Agreement and thus has a license to the Pioneer background CRISPR-Cas9 intellectual property. Under the Intellia Agreement, each party is responsible for 30% of the other party's expenses for prosecution and maintenance of the licensed intellectual property, including 30% reimbursement of the patent prosecution and maintenance costs that we pay to UC/Vienna as described below. The milestones and royalties set forth in the Intellia Agreement are those in the UC/Vienna Agreement and so we pass through any payments received from Intellia to UC/Vienna. The Intellia Agreement continues for the life of the licensed patents and patent applications; provided, however that either party may terminate upon the occurrence of certain events.

In 2018, Intellia initiated an arbitration proceeding over whether two patent families relating, respectively, to CRISPR-Cas9 chRDNA guides and Cas9 scaffolds, were included in the Intellia Agreement. An interim award from the arbitration panel in 2019 determined that both patent families are included in the Intellia Agreement, but the panel granted us an exclusive leaseback to Cas9 chRDNA guides under economic terms to be negotiated by the parties. On June 16, 2021, we entered into a leaseback agreement with Intellia (the "Leaseback Agreement"), which resolved the arbitration proceeding. Pursuant to the Leaseback Agreement, in exchange for Intellia's grant to us of an exclusive license to certain intellectual property relating to CRISPR-Cas9, including Cas9 chRDNAs, for use solely in the manufacture of our CB-010 product candidate, we paid Intellia an upfront cash payment of $1.0 million and will

pay up to $23.0 million in potential future regulatory and sales milestones. Additionally, we will owe Intellia low- to mid- single-digit percent royalties on net sales of our CB-010 product candidate by us, our affiliates, and sublicensees until the expiration, abandonment, or invalidation of the last patent within the intellectual property relating to CRISPR-Cas9, including that relating to Cas9 chRDNAs (i.e., 2036, without PTA or PTE).

The Regents of the University of California ("UC") and the University of Vienna ("Vienna")

On April 16, 2013, we entered into an Exclusive License for Methods and Compositions for RNA-Directed Target DNA Modification and for RNA-Directed Modulation of Transcription with UC and Vienna (as amended, the "UC/Vienna Agreement"), under which we received an exclusive worldwide license, with the right to sublicense, in all fields to the foundational CRISPR-Cas9 patent family co-owned by UC, Vienna, and Dr. Emmanuelle Charpentier (the "CVC IP"). Dr. Charpentier has not granted us any rights to the CVC IP, either directly or indirectly. The UC/Vienna Agreement continues until the last-to-expire patent or last-to-be-abandoned patent application of the CVC IP; provided, however, that UC/Vienna may terminate the UC/Vienna Agreement upon the occurrence of certain events, including our uncured material breach of a material term of the UC/Vienna Agreement, and we may terminate the UC/Vienna Agreement at our sole discretion upon written notice. Without PTA or PTE, the CVC IP will expire in 2033. The UC/Vienna Agreement includes certain diligence milestones that we must meet. For products and services sold by us that are covered by the CVC IP, we will owe low- to mid-single-digit percent royalties on net sales, subject to a minimum annual royalty. Prior to such time that we are selling products, we owe UC/Vienna an annual license maintenance fee. We may owe UC/Vienna up to $3.4 million in certain regulatory and clinical milestone payments in the field of human therapeutics and diagnostics for products developed by us, our affiliates, and sublicensees. Additionally, we pay UC/Vienna a specified percentage of sublicensing revenue we receive including cash and equity under our sublicensing agreements, subject to certain exceptions. If we include intellectual property owned or controlled by us in such sublicense, we pay UC/Vienna a low-double-digit percentage of sublicensing revenues received under the sublicense. If we do not include intellectual property owned or controlled by us in such sublicense, we pay UC/Vienna 50% of sublicensing revenues received under the sublicense. To date, we have entered into over 20 sublicensing agreements in a variety of fields such as human therapeutics, forestry, agriculture, research reagents, transgenic animals, certain livestock targets, internal research, bioproduction, cell lines, and microbial applications that include the CVC IP as well as other Cas9 intellectual property owned or controlled by us. We are obligated to reimburse UC for its prosecution and maintenance costs of the CVC IP. The CVC IP is currently involved in administrative proceedings at the United States Patent and Trademark Office ("USPTO") and at the European Patent Office ("EPO"). See *Risk Factors - "Our ability to continue to receive licensing revenue and to enter into new licensing arrangements related to the foundational CRISPR-Cas9 intellectual property will be substantially impaired if such intellectual property is limited by administrative patent proceeding,*" in Item 1A of this Annual Report on Form 10-K.

On December 15, 2016, we entered into a Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement ("IMA") with UC, Vienna, Dr. Emmanuelle Charpentier, Intellia Therapeutics, CRISPR Therapeutics AG, ERS Genomics Ltd., and TRACR Hematology Ltd. relating to the CVC IP. Under the IMA, each of the owners of the CVC IP (i.e., UC, Vienna, and Dr. Charpentier) retroactively consented to all licenses and sublicenses granted by the other owners and their licensees and also gave prospective consent to any licenses and sublicenses that may be granted in the future. Additionally, the IMA provides for, among other things, (i) good faith cooperation among the parties regarding patent maintenance, defense, and prosecution of the CVC IP; (ii) cost-sharing under which CRISPR Therapeutics AG reimburses us for 50% of what we reimburse UC for patent prosecution and maintenance costs; and (iii) notice of and coordination in the event of third-party infringement of the subject patents and with respect to certain adverse claimants of the CRISPR-Cas9 intellectual property. Unless earlier terminated by the parties, the IMA will continue in effect until the later of the last expiration or abandonment date of the CVC IP.

On March 14, 2019, we entered into a Memorandum of Understanding with UC/Vienna, wherein we agreed that, for sublicensees in the fields of human therapeutics and companion diagnostics, we would pay UC/Vienna the royalties and milestones set forth in the UC/Vienna Agreement for products sold by our sublicensees, not the specified percentage of such sublicensing income received by us. We also agreed to various provisions that must be included in all future sublicensing agreements, including specific provisions for exclusive sublicenses.

Intellectual Property

We strive to protect and enhance the proprietary technologies that we believe are important to our business by seeking patents to cover our platform technologies. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Our success will depend significantly on our ability to obtain and maintain patent and trade secret protection for our technologies, our ability to defend and enforce our intellectual property rights, and our ability to operate without infringing any valid and enforceable intellectual property rights of third parties.

As of March 1, 2022, we own 53 issued U.S. patents, including 8 U.S. patents covering our chRDNA technology; 244 issued foreign patents; and 74 pending patent applications throughout the world. The patent portfolio owned by us includes U.S. and foreign patents and patent applications covering methods and compositions relating to our Cas9 chRDNA and Cas12a chRDNA guides

(which, without PTA or PTE, will expire in 2036). Additionally, our portfolio includes U.S. and foreign patents and patent applications covering methods and compositions relating to the anti-BCMA binding domain of our CB-011 product candidate (which, without PTA or PTE, will expire in 2040). In general, we file our patent applications in the United States and Europe as well as in numerous other foreign patent jurisdictions. We have exclusively in-licensed intellectual property covering the anti-CD371 binding domains of our CB-012 product from MSKCC (which, without PTA or PTE, will expire in 2040).

Additionally, we have extensive patent protection on CRISPR Type I systems, CRISPR-Cas9 methods and compositions, and other genome-editing technologies. The patent term in the United States and other countries is 20 years from the date of filing of the first non-provisional application to which priority is claimed. In the United States, patent term may be lengthened by a PTA, which compensates a patentee for administrative delays by the United States Patent and Trademark Office in granting a patent or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. Additionally, under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Amendments"), the term of a patent that covers an FDA-approved biologic may also be eligible for a PTE of up to five years, which is designed to compensate for the patent term lost during clinical trials and the FDA regulatory review process. A PTE cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent claiming the drug product, methods of use or methods of manufacturing may be restored. Moreover, a patent can only be restored once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved product. Without any PTE, the earliest expiration dates of our granted U.S. patents are in 2032 and the latest expiration dates of our granted U.S. patents are in 2040.

As of March 1, 2022, our trademark portfolio contains 12 trademark registrations, including four U.S. trademark registrations, as well as certain trademark applications. We have registered "CARIBOU," "CARIBOU BIOSCIENCES," "SITE-SEQ," and the Caribou logo as trademarks in relevant classes and jurisdictions in the United States, European Union, and United Kingdom.

Furthermore, we rely upon trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our competitive position. We seek to protect these trade secrets and other proprietary technologies, in part, by entering into confidentiality agreements with parties who have access to them. We also enter into confidentiality and invention assignment agreements with our employees and our agreements with consultants include invention assignment obligations.

Competition

We currently compete across the fields of genome editing and cell therapy. We believe that our novel and proprietary Cas12a chRDNA genome-editing platform has broad potential applicability across human therapeutic indications, and our strategy is to demonstrate our platform's capability by first developing improved allogeneic cell therapies in hematologic oncology indications.

The biopharmaceutical industry, and in particular the genome-editing and cell therapy fields, are characterized by intense investment and competition aimed at rapidly advancing new technologies. Our platform and therapeutic product candidates are expected to face substantial competition from multiple technologies, marketed products, and numerous other therapies being developed by other biopharmaceutical companies, academic research institutions, governmental agencies, and private research institutions. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development staff, established manufacturing capabilities and facilities, and experienced marketing organizations with well-established sales forces. In addition, there is substantial patent infringement litigation in the biopharmaceutical industry and, in the future, we may bring or defend such litigation against our competitors.

Compared to first generation genome-editing approaches, our chRDNA platform has shown improved specificity, a reduction in off-target edits and translocations, and an advanced capability to perform multiplexed edits, in particular multiplexed insertions. Although we believe that our scientific expertise, novel technologies, and intellectual property position offer competitive advantages, we face competition from multiple other genome-editing technologies and companies. Other companies developing CRISPR-based technologies include, among others, Arbor Biotechnologies, Beam Therapeutics Inc., CRISPR Therapeutics AG, Editas Medicine, Inc., Intellia Therapeutics, Inc., Metagenomi Technologies, LLC, and Scribe Therapeutics, Inc. Companies developing other genome-editing technologies include, among others, bluebird bio, Inc., Allogene Therapeutics, Inc., Cellectis S.A., Precision BioSciences, Inc., and Sangamo Therapeutics, Inc.

We believe that our CAR-T cell therapy product candidates have the potential to offer a superior product to patients due to genome edits we make to improve their persistence with the goal of extending robust CAR-T cell antitumor activity in patients. Additionally, our pioneering scientific expertise in iPSC-derived NK cells sets the foundation for our first CAR-iNK cell therapy to target an antigen present on multiple solid tumor malignancies. Due to the promising therapeutic effect of cell therapies, and the

potential benefit of allogeneic treatment alternatives, we expect increasing competition from new and existing companies across four major fronts, which include, among others:

- *Autologous T cell therapy:* 2seventy bio, Inc., Adaptimmune Therapeutics plc, Autolus Therapeutics plc, Bristol-Myers Squibb Company, Gracell Biotechnologies Inc., Kite, a Gilead Company, Lyell Immunopharma, Inc., Novartis International AG, Poseida, TCR2 Therapeutics Inc., and Vor Biopharma Inc.;

- *Allogeneic T cell therapy:* Allogene, Atara Biotherapeutics, Inc., Cellectis, Celyad Oncology SA, CRISPR Therapeutics, Fate Therapeutics, Inc., Gracell, Kite, Legend Biotech Corporation, Poseida, Precision Bio, Sana Biotechnology, Inc., and Vor;

- *Allogeneic NK therapy:* Artiva Biotherapeutics, Inc., Celularity Inc., Century Therapeutics, Editas, Fate, Fortress Biotech, Inc., ImmunityBio, Inc., Nkarta, Inc., NKGen Biotech, Inc., and Takeda Pharmaceutical Company Limited;

- *Other cell therapies:* Other companies are developing CAR-expressing immune cell therapies derived from natural killer T ("NKT") cells, including Kuur Therapeutics; from macrophages, including Carisma Therapeutics; from regulatory T cells, including Kyverna; and from gamma-delta T cells, including Adicet Bio, GammaDelta Therapeutics, Cytomed Therapeutics, TC Biopharm, Hebei Senlang Biotechnology, and Beijing Doing Biomedical Technology Co., Ltd.; and

- *Other oncology therapeutics:* Multiple biotechnology and pharmaceutical companies developing other directly competitive technologies, such as small molecule, antibody, bi-specific antibody, and antibody-drug conjugates.

For a discussion of the risks related to competition, see *Risk Factors - "We face significant competition from other biotechnology and pharmaceutical companies, which may result in other companies developing or commercializing products before, or more successfully than, we do, thus rendering our product candidates non-competitive or reducing the size of our market. Our operating results will suffer if we fail to compete effectively," in Item 1A of this Annual Report on Form 10-K.*

Manufacturing

Manufacturing of both autologous and allogeneic cell therapies requires multiple components and is complex, and there are many similarities in the processes for both kinds of therapies. The advantage of allogeneic therapies is the use of cells from healthy donors and therefore the ability to prepare, qualify, and release clinical material in advance of patient need.

For CB-010, we have optimized the manufacturing process that we developed in-house and have transferred the manufacturing to an external contract manufacturing organization ("CMO") that manufactures current good manufacturing processes ("cGMP")-grade material for our ANTLER phase 1 clinical trial. Additionally, we have developed different analytical methods to understand the integrity of our cells based upon our manufacturing process. We have made a significant investment in process development to facilitate our efforts to improve both the supply chain and our product characterization capabilities.

Figure 24 below describes the process we have developed for the manufacturing of CB-010 CAR-T cells. We use electroporation for the genome-editing step in our process. We use a licensed MaxCyte instrument to achieve high levels of genome

editing at manufacturing scale. Our process includes an important step prior to cryopreservation that significantly removes residual TCR-expressing cells to reduce the likelihood that CB-010 cells will induce GvHD in patients.

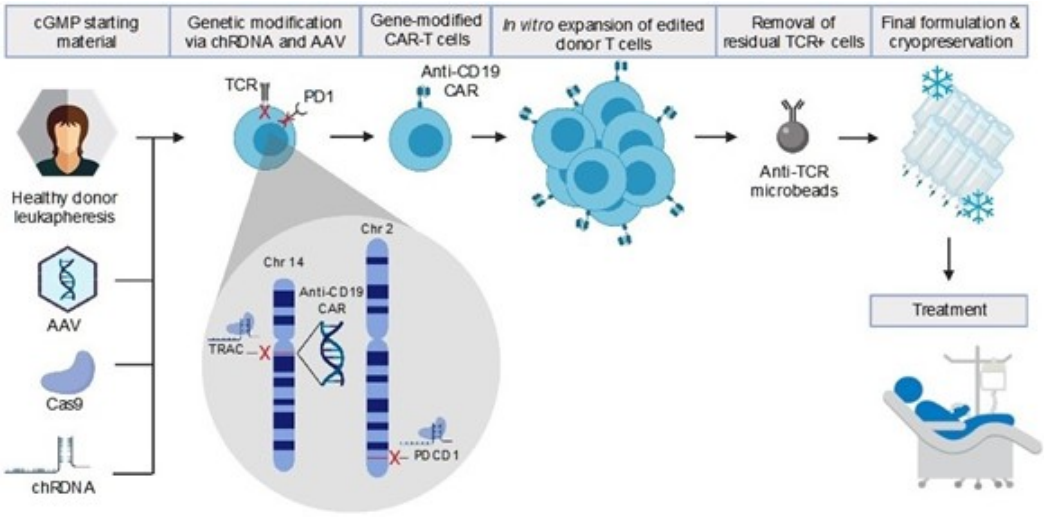


Figure 24. *Our internal process development team developed the manufacturing process for CB-010 and transferred it to a CMO.*

Our process development and manufacturing core competencies and advantages include:

- Standard operating procedures and technologies;
- Process development research from smaller to larger scales;
- Procedures that enable the transfer from process development stage to cGMP conditions;
- Custom engineering to create a robust procedure for each unique pipeline product candidate;
- Removal of residual TCR positive T cells after genome editing to minimize the risk of GvHD in patients;
- Evaluation of all manufacturing steps to optimize for maximal productivity and product integrity;
- Closed manufacturing system;
- Focus on efforts to enhance cell viability;
- Enhancement of gene knockout, CAR expression, and gene insertion;
- Improvements in retaining early memory T cell phenotypes; and
- Approaches to maximizing the number of doses per batch.

The CMO that is manufacturing the phase 1 clinical supply of our CB-010 product candidate is located in the United States and is subject to cGMP requirements, using both qualified equipment and materials. We use multiple CMOs to individually manufacture cGMP chRDNA guides, Cas proteins, and AAV6 vectors used in the manufacture of our CAR-T and CAR-NK cells. We expect to rely on our CMOs for the manufacturing of our product candidates to expedite readiness for future clinical trials, and most of these CMOs have capabilities for commercial manufacturing. Additionally, we may decide to build our own manufacturing facility in the future to provide us greater flexibility and control over our clinical or commercial manufacturing needs.

Government Regulation

As a biotechnology company, we are subject to extensive legal and regulatory requirements. For example, we may need approval from regulatory agencies for our research, development, testing, manufacture, quality control, approval, packaging, storage,

record keeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of our product candidates. Relevant regulatory authorities include, but are not limited to, the FDA, the European Medicines Agency ("EMA"), an agency of the European Union ("EU") in charge of the evaluation and supervision of medicinal products; the European Commission, which is the executive arm of the EU; and other national, state, local, and provincial regulatory authorities. The United States and certain jurisdictions outside the United States also regulate the pricing and reimbursement of such products. The processes for obtaining marketing approvals in the United States and in other countries and jurisdictions, along with subsequent 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, our product candidates are regulated as biological products, or biologics, under the Public Health Service Act (the "PHSA"), and the Federal Food, Drug, and Cosmetic Act (the "FDCA"), and their implementing regulations promulgated by the FDA. The failure to comply with the applicable requirements at any time during the product development process, including nonclinical testing, clinical testing, the approval process, or post-approval process, may subject us to delays in the conduct of a clinical trial, regulatory review and approval, and/or subject us to administrative or judicial sanctions. Such sanctions may include, but are not limited to, the FDA's refusal to allow us to proceed with clinical testing of our product candidates, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, receipt of untitled or 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, U.S. Department of Justice ("DOJ"), or other governmental entities.

As we seek approval to market and distribute a new biologic in the United States, we generally must satisfactorily complete each of the following steps:

- preclinical laboratory tests, animal studies, and formulation studies all performed in accordance with the FDA's current Good Laboratory Practice ("cGLP") regulations;
- manufacture and testing of clinical investigational product according to cGMPs;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board ("IRB"), representing each clinical trial site before each clinical trial may be initiated, or by a central IRB if appropriate;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication, in accordance with the FDA's current Good Clinical Practice ("cGCP") regulations including, but not limited to, informed consent and investigator disclosure requirements;
- preparation and submission to the FDA of a BLA for marketing approval of our product candidates for one or more proposed indications, including submission of detailed information on the manufacture and composition of our product candidates and proposed labeling;
- review of the BLA by an FDA advisory committee, where applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities, including those of any third-party manufacturers, at which the product, or components thereof, are produced in order to assess compliance with cGMP requirements and to ensure that the facilities, methods, and controls are adequate to preserve and ensure the product's identity, strength, quality, and purity, and, if applicable, the FDA's current Good Tissue Practice ("cGTP"), for the use of human cell and tissue products;
- satisfactory completion of any FDA audits of the nonclinical study and clinical trial sites to ensure compliance with cGLPs and cGCPs, respectively, and the integrity of nonclinical and clinical data in support of the BLA;
- payment of user fees and securing FDA approval of the BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy ("REMS") adverse event reporting, and compliance with any post-approval studies required or requested by the FDA.

Preclinical Studies and Investigational New Drug Application

Before testing any investigational biologic product candidate in humans, our product candidates must undergo preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, formulation, and stability, as well as studies to evaluate the potential for safety, efficacy, and toxicity in animals. The conduct of the preclinical tests and the formulation of the compounds for use in the preclinical testing must comply with federal regulations and/or requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application. An IND is an exemption from the restrictions of the FDCA, which would otherwise preclude an unapproved biologic product candidate from being shipped in interstate commerce. Under an approved IND, the unapproved biologic product candidate may be shipped in interstate commerce for use in an investigational clinical trial, provided that the product candidate meets certain quality and labeling requirements. The FDA has 30 calendar days after receipt of our IND application to review and decide whether we may proceed to human clinical trials. During or after its review, the FDA may raise concerns or questions about our product candidate or conduct of the proposed clinical trial, including concerns that human research subjects could be exposed to unreasonable and significant health risks. If the FDA raises concerns or questions during this 30-day period, including safety concerns or concerns due to regulatory non-compliance, we and the FDA must resolve any outstanding concerns before the clinical trials can begin. In certain cases, the FDA may impose a partial or complete clinical hold with respect to our product. Such a clinical hold would delay either a proposed clinical trial, or cause suspension of an ongoing clinical trial, until all outstanding concerns have been adequately addressed, and the FDA has notified us that our clinical trials may proceed or recommence. In certain cases, we may not be able to proceed at all with our proposed clinical trial.

Human Clinical Trials in Support of a BLA

Our clinical trials involve the administration of our product candidate to patients with the disease to be treated and are conducted under the supervision of a qualified principal investigator in accordance with cGCP requirements. Clinical trials are conducted under study protocols detailing, among other things, the objectives of the clinical trial, inclusion, and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and subsequent protocol amendments must be submitted to the FDA as part of the IND and must also be reviewed by an IRB.

If we wish to conduct a clinical trial outside of the United States, we may, but need not, obtain FDA authorization to conduct the clinical trial under an IND application. When a foreign clinical trial is conducted under a foreign equivalent to an IND application, all FDA IND applications requirements must be met unless waived. If a non-United States clinical trial is not conducted under a U.S. FDA IND application, we may submit data from a well-designed and well-conducted clinical trial to the FDA in support of our BLA, so long as the clinical trial is conducted in compliance with cGCP and the FDA is able to accept the data from the clinical trial and/or through an onsite inspection if the FDA deems it necessary. In certain cases, however, the FDA may refuse to approve drugs based only on clinical trials conducted outside of the United States. For example, an FDA panel recently recommended against approving an immunotherapy drug that was tested only in China, citing potential concerns about the diversity of the clinical trial population, among others. A senior FDA official has also voiced concerns recently about approving drugs that are developed and tested only in overseas markets. It is not clear how or whether FDA's policies may change in the future.

For clinical trials conducted in the United States, each clinical trial must be reviewed and approved by an IRB, either centrally or individually at each institution at which our clinical trials will be conducted. The IRB will consider, among other things, our clinical trial design, subject informed consent, ethical factors, and the safety of human subjects. The IRB must operate in compliance with FDA regulations governing IRBs. The FDA, the applicable IRB, or we may suspend or terminate a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements or that the subjects or patients are being exposed to an unacceptable health risk. Some clinical trials receive additional oversight by an independent group of qualified experts organized by us, known as a data safety monitoring board or committee. This group receives and reviews data arising from the clinical trial on an ongoing basis and may recommend continuation of the clinical trial as planned, changes in clinical trial conduct, or cessation of the clinical trial at designated check points based on such data.

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

Institutes of Health ("NIH") funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

Clinical trials typically are conducted in three sequential phases; however, the phases may overlap or may be combined.

- Phase 1 clinical trials are initially conducted in a limited population of healthy humans or, for our product candidates, in patients, such as cancer patients, in order to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics, and to identify a recommended phase 2 dose.

- Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications, and to determine dose tolerance and optimal dosage. We may conduct multiple phase 2 clinical trials to obtain information prior to beginning larger and costlier phase 3 clinical trials. The phase 2 clinical trial for our product candidates may serve as the pivotal trial, in which case a phase 3 clinical trial will not be necessary.

- Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage and gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the status of clinical trials must be submitted to the FDA. Written IND safety reports must be submitted to the FDA and the investigators within 15 calendar days of receipt by us after determining that the information qualifies for such expedited reporting. IND safety reports are required for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk to humans in our clinical trials, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Additionally, we must notify FDA within seven calendar days after receiving information concerning any unexpected fatal or life-threatening suspected adverse reaction. Other external events may occur that can affect the conduct of our clinical trials, such as pandemics or government shutdowns.

In some cases, the FDA may approve a BLA for our product candidate but require us 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 patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. Failure to exhibit due diligence in conducting phase 4 clinical trials could result in withdrawal of approval for our products.

Guidance Governing Gene Therapy Products

The FDA has defined a gene therapy product as one that mediates its effects by transcription and/or translation of transferred genetic material or by specifically altering host (human) genetic sequences. Examples of gene therapy products include nucleic acids (e.g., plasmids, *in vitro* transcribed ribonucleic acid), genetically modified microorganisms (e.g., viruses, bacteria, fungi), engineered site-specific nucleases used for human genome editing, and *ex vivo* genetically modified human cells. The products may be used to modify cells *in vivo* or transferred to cells *ex vivo* prior to administration to the recipient. Within the FDA, the Center for Biologics Evaluation and Research ("CBER") regulates gene therapy products. Within CBER, the review of gene therapy and related products is consolidated in the Office of Tissues and Advanced Therapies, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. The FDA and the NIH have published guidance documents with respect to the development and submission of gene therapy protocols.

Although the FDA has indicated that its guidance documents regarding gene therapies are not legally binding, we believe that our compliance with them is likely necessary to gain approval for any product candidate we may develop. The guidance documents provide additional factors that the FDA will consider at each of the above stages of development and relate to, among other things, the proper preclinical assessment of gene therapies; the chemistry, manufacturing, and control information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; 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. Depending on the product type, long term follow up can be up to 15 years or as short as five years.

Clinical Trial Registry

There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries, such as such as *www.ClinicalTrials.gov.* We are required to register and disclose certain clinical trial information, including the product information, patient population, phase of investigation, clinical trial sites and investigators, and other aspects of the clinical trial on *www.ClinicalTrials.gov*. We are also obligated to disclose the results of our clinical trials after completion. Disclosure of the results of these clinical trials can be delayed until the new product candidate or new indication being studied has been approved, up to a maximum of two years.

Compliance with cGMP and cGTP requirements

Before approving a BLA, the FDA typically will inspect the facility or facilities where our product candidates are manufactured. The FDA will not approve a BLA unless it determines that the manufacturing processes and facilities are in full compliance with cGMP requirements and adequate to ensure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing control for products such as biologics whose attributes cannot be precisely defined. Material changes in manufacturing equipment, location, or process post-approval may result in additional regulatory review and approval.

The FDA also will not approve the product if we are not in compliance with cGTPs, which are requirements found in FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue-based products ("HCT/Ps"), which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the cGTP requirements is to ensure that cell- and tissue-based products are manufactured in a manner designed to prevent the introduction, transmission, and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing.

Review and Approval of a BLA

The results of product candidate development, preclinical testing, and clinical trials, including negative or ambiguous results as well as positive findings, are submitted to the FDA as part of a BLA requesting a license to market the product. The BLA must contain extensive manufacturing information and detailed information on the composition of the product candidate and proposed labeling as well as payment of a user fee.

The FDA has 60 calendar days after submission of a BLA to conduct an initial review to determine whether the BLA is acceptable for filing based on the agency's threshold determination that the BLA is sufficiently complete to permit substantive review. Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act ("PDUFA"), the FDA has 10 months in which to complete its initial review of a standard application and respond to us, and six months for a priority review of the application. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs. The review process may often be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may be extended by three months if the FDA requests, or if we otherwise provide through the submission of a major amendment, additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Under the PHSA, the FDA may approve a BLA if it determines that our product candidate is safe, pure, and potent and the manufacturing facility meets standards designed to ensure that our product continues to be safe, pure, and potent.

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of nonclinical study and clinical trial sites to ensure compliance with cGMPs and cGCPs, respectively, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of our product candidate with specific prescribing information for specific indications. If our BLA is not approved, the FDA will issue a complete response letter, which will contain the conditions that must be met in order to secure final approval of the application and, when possible, will outline recommended actions we might take to obtain approval of our BLA. If we receive a complete response letter, we may submit to the FDA information that represents a complete response to the issues identified by the FDA. Such resubmissions are classified under the PDUFA as either Class 1 or Class 2. The classification of a resubmission is based on the information submitted by us in response to the complete response letter. Under the goals and policies agreed to by the FDA under the PDUFA, the FDA has two months to review a Class 1 resubmission and six months to review a Class 2 resubmission. The FDA will not approve an application until issues identified in the complete response letter have been addressed. Alternatively, if we receive a complete response letter, we may either withdraw our BLA or request a hearing.

The FDA may also refer our BLA to an advisory committee for review, evaluation, and recommendation as to whether our BLA should be approved. In particular, the FDA may refer to an advisory committee application for biologic products that present

difficult questions of safety or efficacy. 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.

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

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

The FDA is authorized to designate certain products for expedited review if such products are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include fast track designation, breakthrough therapy designation, priority review, and regenerative medicine advanced therapy designation. These designations are not mutually exclusive, and our product candidates may qualify for one or more of these programs. Although these programs are intended to expedite product development and approval, they do not alter the standards for FDA approval.

The FDA may designate our product candidate for fast track review if our product candidate 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 can be demonstrated that our product candidate has the potential to address unmet medical needs for such a disease or condition. For fast track product candidates, we may have greater interactions with the FDA, and the FDA may initiate review of sections of our fast track product candidate'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 us, that a fast track product candidate may be effective. We must also provide, and the FDA must approve, a schedule for the submission of the remaining information, and we must pay applicable application 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, or if our designated product candidate development program is no longer being pursued.

Our product candidates may obtain breakthrough therapy designations if they are 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 our product candidates 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 product candidates with such designations, including holding meetings with us throughout the development process, providing timely advice to us 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. Breakthrough designation may be rescinded if our product candidate no longer meets the qualifying criteria.

The FDA may designate our product candidate for priority review if our product candidate treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness of the treatment, prevention, or diagnosis of such condition. The FDA makes such determination on a case-by-case basis, 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 adverse 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 acting on a marketing application from 10 months to six months.

The FDA may designate our product candidates as regenerative medicine advanced therapies ("RMAT") if our product candidates are regenerative medicine therapies intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that our product candidates have the potential to address unmet medical needs for such disease or condition. RMAT designation provides potential benefits that include early interactions and more frequent meetings with the FDA to discuss the development plan for the product candidate and eligibility for rolling review and priority review. Product candidates granted RMAT designation may also be eligible for accelerated approval on the basis of surrogate or intermediate

clinical trial endpoints reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. RMAT-designated products that receive accelerated approval may, as appropriate, fulfill their post-approval requirements through the submission of clinical evidence, clinical trials, patient registries, or other sources of real-world evidence such as electronic health records, through the collection of larger confirmatory data sets as agreed with the FDA, or via post-approval monitoring of all patients treated with such therapy prior to approval of the therapy. Regenerative medicine advanced therapy designation may be rescinded if our product candidate no longer meets the qualifying criteria

Accelerated Approval Pathway

The FDA may grant accelerated approval to our product candidates for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that our 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 our product candidate has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality ("IMM"), and that our product candidate 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. Product candidates granted accelerated approval must meet the same statutory standards for safety and efficacy 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 product candidate, 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 could support accelerated approval where a clinical trial demonstrates a relatively short-term clinical benefit in a chronic disease setting in which assessing durability of the clinical benefit is essential for traditional approval, but the short-term benefit is considered reasonably likely to predict long-term benefit.

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 candidate, 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.

The accelerated approval pathway is usually contingent on our agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe our product candidate's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of 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 withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA unless the FDA informs us otherwise.

Post-Approval Regulation

If regulatory approval for marketing of any of our product candidates is obtained, we will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA has imposed as part of the approval process. We will be required to report certain adverse reactions and manufacturing problems to the FDA, provide updated safety and efficacy information, and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers of our products are required to register their establishments with the FDA and certain state agencies and are subject to periodic announced or ad hoc 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 these manufacturers. Accordingly, we and our 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.

Our products may also be subject to official lot release, meaning that the manufacturer of our products is required to perform certain tests on each lot of the product before the product is released for distribution. If the product is subject to official lot release, the manufacturer must submit to the FDA samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of the manufacturer's tests performed on the lot. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution.

Once a marketing approval is granted for our product candidate, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after our product reaches the market. Later discovery of previously unknown problems with our product, including adverse events of unanticipated severity or frequency, issues with manufacturing

processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-marketing studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS program.

Other potential consequences of a failure to comply with regulatory requirements include:

- restrictions on the marketing or manufacturing of our product, complete withdrawal of our product from the market, or product recalls;
- fines, untitled or warning letters, or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of our product license approvals;
- product seizure or detention, or refusal to permit the import or export of products or the raw materials or ingredients that are needed for product manufacture; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of licensed and approved products that are placed on the market. Pharmaceutical products may be promoted only for the approved indications and in accordance with the provisions of the approved label.

Orphan Drug Designation

Orphan drug designation may be available for drugs that are intended for rare diseases or conditions, defined as (i) a disease or condition that affects fewer than 200,000 individuals in the United States or (ii) a disease or condition that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available a biologic for the disease or condition will be recovered from sales of the product in the United States. If a drug becomes the first drug that is approved for the same indication for which the FDA has granted the designation, the drug will be entitled to exclusivity, which means the FDA may not approve any other application to market the same drug for the same orphan indication for a period of seven years following the date of our product's marketing approval, except in certain circumstances. In addition, other financial incentives, such as tax credits, may be available. To obtain orphan drug designation, we must make a request before submitting our BLA for a particular product candidate. After the FDA grants orphan drug designation, the generic or trade name, or the chemical name or a meaningful description of the biologic, its designated orphan use and date of designation, and our company name 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. We have not requested, or received, an orphan drug designation for any of our product candidates. However, we may request such a designation in the future.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003 (as amended, "PREA"), a BLA or supplement to a BLA for a product candidate with certain novel characteristics must contain data to assess the safety and effectiveness of the product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product candidate is safe and effective.

Sponsors must submit a pediatric study plan to FDA outlining the proposed pediatric study or studies they plan to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The FDA must then review the information submitted, consult with the sponsor, and agree upon a final plan. The FDA or the sponsor 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 a sponsor, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with the sponsor and the FDA must meet with the sponsor by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than 90 calendar days after FDA's receipt of the study plan. The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements, under specified circumstances. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

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 pediatric data is submitted that sufficiently responds to a written request from the FDA for such data. The data do not need to show a product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to be responsive 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 PTE; instead, this grant of exclusivity extends the regulatory period during which the FDA cannot approve another application.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (the "Affordable Care Act") includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (the "BPCIA"), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product in the United States. Starting in 2015, the FDA commenced licensing biosimilars under the BPCIA, and there are currently numerous biosimilars approved in the United States and Europe.

For the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, 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 efficacy relative to exclusive use of the reference biologic. Even after the FDA approves a biosimilar product, the product, its manufacturing processes, post-approval clinical data, labeling, advertising, and promotional activities for the product will be subject to continuous requirements of and review by the FDA or other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, including mandatory post-marketing safety reporting; registration and listing requirements; cGMP requirements relating to quality control, quality assurance, and corresponding maintenance of records and documents; and requirements regarding recordkeeping.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. 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 approves a full BLA for such product containing our own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of the product.

Patent Term Extension

A patent claiming a new biologic product may be eligible for a limited PTE under the Hatch-Waxman Amendments, 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 BLA, plus the time between the submission date of a BLA and the ultimate approval date, less any time during which due diligence was not conducted. PTE cannot be used to extend the remaining term of a patent past a total of 14 years from the product's regulatory approval date. Pursuant to 35 U.S.C. § 156, only one patent covering an approved product, or the use or manufacture thereof, is eligible for PTE, and the application for the extension must be submitted prior to the expiration of the patent in question and within 60 calendar days after regulatory approval. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any PTE in consultation with the FDA. Similar provisions are available in Europe and other jurisdictions to extend the term of a patent that covers an approved biologic although the eligibility requirements for these extensions vary.

Regulation and Procedures Governing Approval of Medicinal Products in Other Countries

In order to market any product outside of the United States, we must also comply with numerous and comprehensive regulatory requirements of other countries and jurisdictions, regarding quality, safety, and efficacy, and governing, among other things, clinical trials, marketing authorization, post-authorization requirements, commercial sales, import and export, reimbursement, and distribution of products. Whether or not we obtain FDA approval for our product candidates, we will need to obtain the necessary approvals from the comparable health regulatory authorities in other countries or jurisdictions before we can initiate clinical trials or marketing of our products 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 EU, either at all or within the same timeframe as approval may be granted in the United States. The process entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of a product candidate for each proposed indication. It also requires the submission to the EMA or the

relevant member state competent authorities, of a marketing authorization application and granting of a marketing authorization by the EMA or these authorities before the product can be marketed and sold in the EU.

U.S. Export Control Licensing Requirements and Other U.S. and Foreign Trade Regulations, Sanctions Laws, Anti-Corruption, and Anti-Money Laundering Laws

We develop product candidates that may be subject to varying U.S. export control licensing requirements and foreign investment regulations. In addition, U.S. international trade laws, including the U.S. Foreign Corrupt Practices Act of 1977, as amended ("FCPA"), and similar anti-bribery or anti-corruption laws, regulations, and rules of other countries in which we may choose to operate, could apply to our international activities. Anti-corruption laws generally prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector in order to influence action. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the company and to devise and maintain an adequate system of internal accounting controls.

In addition, U.S. import and export regulations, anti-money laundering laws, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls could apply to any international activities we may undertake.

Coverage, Pricing, and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may seek regulatory approval by the FDA or other government authorities. In the United States and other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services often rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use any product candidates we may develop unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such product candidates. In addition, direct or indirect governmental price regulation may affect the prices that we may charge for product candidates.

United States

Even if any product candidates we may develop obtain approval, sales of such product candidates will depend, in part, on the extent to which third-party payors, including government healthcare 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 such product candidates.

In general, factors a payor considers in determining coverage and reimbursement are based on whether the product is:

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

In the United States, no uniform policy of coverage and reimbursement for biological products, including gene and cell therapy products, exists among third-party payors. As a result, obtaining coverage and reimbursement approval for such a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical, and cost-effectiveness data regarding the products' clinical benefits, medical necessity, and risks on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. A decision by a third-party payor not to cover any product candidates we may develop could reduce physician utilization of such product candidates once approved and have a material adverse effect on our 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 approved, and inadequate reimbursement rates, including significant patient cost sharing obligations, may deter patients from selecting our product candidates. One payor's determination to provide coverage for a product does not ensure 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. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and

reimbursement status is attained for one or more products for which we receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

European Union

In the EU, the approval process and requirements governing pricing and reimbursement for any product candidate vary greatly between countries and jurisdictions. Some countries allow biological products to be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional testing or studies that compare the cost effectiveness of a particular biological product to currently available treatments, or so-called health technology assessments, in order to obtain reimbursement or pricing approval.

Some countries, including several EU member states, set prices and reimbursement for biological products, with limited participation from the marketing authorization holders. For example, the EU provides options for its member states to restrict the range of biological products for which their national health insurance systems provide reimbursement and to control the prices of biological products for human use. EU member states may approve a specific price for a biological product or may instead adopt a system of direct or indirect controls on the profitability of the company providing the biological product. Recently, many European countries have increased the level of discounting required in relation to the pricing of biological products and these efforts could continue as countries attempt to manage healthcare expenditures.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of pharmaceutical products that are granted marketing approval. Arrangements with providers, consultants, third-party payors, customers, and patients are subject to broadly applicable fraud and abuse laws including anti-kickback laws, false claims laws, and health care provider payment transparency laws, as well as data privacy and security laws and other healthcare laws that may constrain our business and/or financial arrangements.

Restrictions under applicable federal and state healthcare laws and regulations, include but are not limited to the following:

- the U.S. federal Anti-Kickback Statute (“AKS”), which prohibits, among other things, individuals or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce, or reward, either the referral of an individual, or the purchase, lease, order, arrangement for or recommendation of the purchase, lease, order, arrangement for any good, facility, item, or service, for which payment may be made, in whole or in part, under a federal healthcare program, such as Medicare and Medicaid;

- the U.S. civil and criminal false claims laws, including the civil United States 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 be made or used a false record or statement to avoid, decrease, or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the AKS or FDA promotional standards constitutes a false or fraudulent claim for purposes of the United States False Claims Act;

- the U.S. federal Beneficiary Inducement Statute, which prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value, with limited exceptions, to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary’s selection of a particular provider, practitioner, or supplier of items or services reimbursable by a federal or state health program;

- the U.S. Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”), and their respective implementing regulations (collectively “HIPAA”), which imposes criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private payors, or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services;

- HIPAA also imposes obligations with respect to safeguarding the privacy, security, and transmission of individually identifiable information that constitutes protected health information, including mandatory contractual terms and restrictions on the use and/or disclosure of such information without proper authorization;

- the federal transparency requirements known as the U.S. Physician Payments Sunshine Act, or Open Payments program, created under the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics, and medical supplies to report annually to the Centers for Medicare & Medicaid Services ("CMS") information related to payments, including certain product development activities such as clinical trials, and other transfers of value made by that entity to covered recipients, currently defined to include doctors, dentists, optometrists, podiatrists, chiropractors, teaching hospitals, physician assistants, nurse practitioners, and certain other healthcare providers and requires certain manufacturers and applicable group purchasing organizations to report ownership and investment interests held by physicians or their immediate family members;

- U.S. price reporting laws, which require companies to calculate and report complex pricing metrics in an accurate and timely manner to government programs. Such laws may not only affect coverage, reimbursement, and pricing for our product candidates, but can also result in civil penalties for late or incorrect reports;

- U.S. consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- the FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- certain state and other laws that require pharmaceutical companies to comply with the state standards or pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. government in addition to requiring pharmaceutical manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures;

- certain state and other laws that 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; and

- analogous state and foreign laws and regulations, which may be broader in scope than their federal equivalents.

Numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our collaborators and third-party providers. California has enacted the California Consumer Privacy Act (the "CCPA"). The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Additionally, the California Privacy Rights Act amended the CCPA to impose additional data protection obligations on companies doing business in California, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, opt outs for certain uses of sensitive data, and creation of a new California data protection agency authorized to issue substantive regulations. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. In the United States, states are constantly amending existing laws, requiring attention to frequently changing regulatory requirements.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years that apply to the pricing of pharmaceutical and biopharmaceutical products, limit coverage and reimbursement for drugs and other medical products, require substitution of generic products, standardize access to third-party insurance coverage, and address government control and other changes to the healthcare system in the United States. The federal and state governments may pass legislation designed to reduce the cost of healthcare, and future amendments and new proposals may affect the commercialization of any of our product candidates in ways that we cannot foresee.

For example, in March 2010, the United States Congress enacted the Affordable Care Act, which, among other things, included changes to the coverage and payment for products under government health care programs.

Among the provisions of the Affordable Care Act that may be of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price" for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 70% point-of-sale-discount off the negotiated price of applicable products to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient products to be covered under Medicare Part D, increased pursuant to the Bipartisan Budget Act;
- the establishment of a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the establishment of the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription product spending;
- introduction of a new average manufacturer price definition for biologics and drugs that are inhaled, infused, instilled, implanted, or injected and not generally dispensed through retail community pharmacies;
- increase in the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and expansion of rebate liability from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well;
- establishment of a branded prescription drug fee that pharmaceutical manufacturers of branded prescription drugs must pay to the federal government;
- expansion of the list of covered entities eligible to participate in the 340B drug pricing program;
- 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 individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; and
- creation of a licensure framework for follow on biologic products.

Recently, CMS finalized regulations that give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the Affordable Care Act for plans sold through such marketplaces. It is unclear what type of impact, if any, efforts such as this will have on our business in the future.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers, and cancer treatment centers, and increased from three to five years the statute of limitations period for the government to recover non-fraudulent overpayments to providers. New laws may result in additional reductions in Medicare and other healthcare funding, which may materially adversely affect customer demand for and affordability of our product candidates and, accordingly, our business, financial condition, results of operations, and prospects. Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, which first affected physician payment in 2019. At this time, it is unclear how the introduction of the Medicare quality payment program will impact overall physician reimbursement.

Beyond the Affordable Care Act, other legislative measures have also been enacted that may impose additional pricing and product development pressures on our business. For example, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain IND products that have completed a phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug product candidates available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy. We expect that additional foreign, federal, and state 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 limited coverage and reimbursement and reduced demand for our products, post-approval, or additional pricing pressures. Individual states in the United States have also become increasingly active in enacting 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. We cannot predict what healthcare reform initiatives may be adopted in the future. Additional federal, state, and foreign legislative and regulatory developments are likely, and we expect ongoing initiatives to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates and may affect our overall financial condition and ability to develop product candidates.

Additional Regulations

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the U.S. Occupational Safety and Health Act, the U.S. Resource Conservancy and Recovery Act, and the U.S. Toxic Substances Control Act, all affect our business. These and other state and local laws govern our use, handling, and disposal of various biological, chemical, and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines.

Employee and Human Capital Resources

Overview

As of March 1, 2022, we had 97 employees. Of these employees, 73% are primarily engaged in research and development activities and 55% of our research and development personnel have one or more advanced degrees. None of our employees is represented by a labor union or party to a collective bargaining agreement. We consider our relationship with our employees to be good.

We have attracted a talented group of experienced scientists, drug development experts, and company builders as part of a passionate team of employees. Our research and development team includes scientists, engineers, and clinicians who are experts in genome-editing technologies, cellular engineering, computational biology, genome sequencing and analysis, structural biology, chemistry, lab automation, translational medicine, and the manufacturing of CRISPR reagents and cell therapies. Our team of employees includes many scientists who invented the technologies we use today in our research and product development and who continue to drive innovation.

We recognize that attracting, motivating, and retaining talent at all levels is vital to our continued success. Our employees are a significant asset and we aim to create an equitable, inclusive, and empowering environment in which our employees can grow and advance their careers, with the overall goal of developing, expanding, and retaining our workforce to support our current pipeline and future business goals. By focusing on employee retention and engagement, we also improve our ability to support our clinical trials, our pipeline, our platform technologies, and our business and operations, while protecting the long-term interests of our stockholders. Our success depends on our ability to attract, engage, and retain a diverse group of employees. We value innovation, passion, data-driven decision making, persistence, and honesty, and we are building an inclusive environment where our employees can thrive and be inspired to make exceptional contributions to bring therapies to patients.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, motivating, and integrating our existing and future employees. The principal purposes of our equity and cash incentive plans are to attract, retain, and motivate employees through grants of stock-based compensation awards and payments of performance-based cash bonus awards, which motivate our employees to perform to the best of their abilities and achieve our objectives. We are committed to providing a competitive and comprehensive benefits package to our employees. Our benefits package provides a balance of overall protection along with the flexibility to meet the individual health and wellness needs of our employees. We plan to continue to refine our efforts related to optimizing our use of human capital as we grow, including improvements in the way we hire, develop, motivate, and retain employees.

Since the start of the COVID-19 pandemic, we have been and will continue to be focused on the safety of our employees. In response to the COVID-19 pandemic, we have instituted on-site protocols and procedures in accordance with regulations and guidelines promulgated by the Centers for Disease Control, the State of California, the California Department of Public Health, the California Occupational Health and Safety Administration, the County of Alameda, and the City of Berkeley. All of our employees are required to be fully vaccinated against COVID-19 as a condition of working with us. Individuals who are unable to be vaccinated, due to a religious belief, a medical condition, or disability that prevents them from being vaccinated, can request a reasonable accommodation.

Diversity, Equity, and Inclusion

We are committed to cultivating, fostering, and preserving a culture of diversity, equity, and inclusion ("DEI"). We foster an inclusive environment through respect, collaboration, and candid communication. We embrace and encourage differences in age, color, disability, ethnicity, family or marital status, gender identity or expression, language, national origin, culture or customs, physical and mental ability, political affiliation, race, religion, sexual orientation, socio-economic status, veteran status, and other characteristics that make our employees unique. We embrace differences in experience and background, and we welcome a diversity of opinions when making decisions. We would not be who we are today without the diversity of our team.

As of March 1, 2022, 55% of our employees self-reported as female. The ratio of men to women is fairly balanced at each level of our organization; as an example, 58% of our director-level and above employees self-reported as female and 42% of this group self-reported as male. In addition, as of March 1, 2022, 46% of our employees self-reported as ethnic or racial minorities, with 27% self-identifying as Asian, 3% Black or African American, 7% Hispanic or Latinx, and 8% of other minority groups or two or more races; 46% of our director-level and above employees self-reported as ethnic or racial minorities. Our employees span multiple age brackets and bring their unique perspectives and experiences to our organization. As of March 1, 2022, the average age of our employees is 40.8 years old, 52% of our workforce is under 40 years of age, and 48% of our workforce is 40 years of age or older. Although we are proud of our efforts and metrics to date, we recognize that there is still more work to be done until the diversity of our workforce matches the diversity of the Bay Area.

To champion our efforts in this area, in 2021 we formed an Inclusion Committee comprised of employees from various departments, backgrounds, and levels within our organization. The Inclusion Committee emphasizes our commitment to the importance of DEI and the responsibility of our employees to treat others with dignity and respect at all times. All employees are provided diversity awareness training and unconscious bias training to enhance their knowledge to fulfill this responsibility, in addition to mandatory sexual harassment prevention training. The Inclusion Committee works to identify gaps, respond to feedback provided by peers and present suggestions on our hiring and retention practices and policies to encourage and enforce an environment in which all employees feel included and empowered to achieve their best. Management has committed time and resources for this ongoing initiative.

Involvement in Our Community

Our headquarters are located in Berkeley, California, and many of our employees are alumni of local universities and some have grown up in the San Francisco Bay Area and attended local schools. Our employees are talented and passionate people who are committed to making a difference in our community and beyond. As a company, we actively participate in outreach efforts to increase opportunities for underrepresented groups, including hosting and providing volunteers for science, technology, engineering, and mathematics ("STEM") programs at local elementary, junior high, and high schools as well as community colleges and universities. Many of our employees speak at local schools about careers in biotechnology and we have hosted students at our facility to engage them in aspects of biotechnology to which they may not have been previously exposed. We look for opportunities to foster the growth of future scientists and a love of science. We provide each of our employees with eight hours of paid volunteer time each year, which can be used for participating in school activities, voter registrations, environmental activities, and the like.

We are environmentally conscious. With this in mind, we strive to mitigate our impact on the environment where possible and pursue innovative ways to grow our business while minimizing our environmental footprint. The City of Berkeley requires companies with 10 or more employees to have a commuter benefits program in place, and we offer pre-tax commuter benefits to ride public transportation, which is connected to our facility through various free shuttle services. Additionally, we provide bicycle vouchers to employees who bike to work and have bike repair tools on site as well as bike storage areas. Our facility is equipped with water stations that filter water to discourage the use of plastic bottles. All refuse generated at our company is sorted among recycle, compost, and landfill. We have already moved to electronic documentation and files in many functions and are in the process of completing our transition to a mostly paperless workplace.

The Herd at Caribou

We at Caribou refer to ourselves as "the herd." We encourage and value social interactions among the herd. To this end, until the COVID-19 pandemic, we met for quarterly events, including a company-organized San Francisco Bay shoreline clean-up effort. During the COVID-19 pandemic, we held quarterly events virtually, such as chocolate tastings and ramen cooking. We also sponsor a monthly "fun run" for employees to either run or walk to the shoreline or in the Berkeley hills. For several years, we have offered yoga for our employees, and we have continued this virtually during the COVID-19 pandemic.

Information Available on the Internet

Investors and others should note that we announce material information to our investors using our investor relations website (https://cariboubio.com/investors), our filings with the Securities and Exchange Commission (the "SEC"), press releases, public conference calls, and webcasts. We use these channels to communicate with the public about our company, our business, our product candidates and other matters. 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) and 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), are available on our website free of charge as soon as reasonably practicable after we electronically file the material with, or furnish it to, the SEC. The materials we file with or furnish to the SEC are also available at http://www.sec.gov.

Item 1A. Risk Factors.

Investing in shares of our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all of the other information contained in this Annual Report on Form 10-K, including our financial statements and related notes, before making an investment decision. The risks described below are not the only ones facing us. The occurrence of any of the following risks, or of additional risks and uncertainties not presently known to us or that we currently believe to be immaterial, could materially and adversely affect our business, financial condition, results of operations and prospects, and reputation. In such case, the trading price of shares of our common stock could decline, and you may lose all or part of your investment. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of a number of factors, including the risks described below. See Special Note Regarding Forward-Looking Statements in this Annual Report on Form 10-K.

Risks Relating to Our Financial Position and Need for Additional Capital

We have incurred significant net losses since our inception and anticipate that we will incur continued net losses for the foreseeable future.

We have incurred significant net losses each year since our inception. For the years ended December 31, 2021 and 2020, we incurred net losses of $66.9 million and $34.3 million, respectively. As of December 31, 2021, we had an accumulated deficit of $97.8 million. In addition, we have not commercialized any products and have never generated any revenue from product sales. We have devoted almost all of our financial resources to research and development, including our preclinical development activities.

We expect to continue to incur significant expenses and net losses over the next several years and for the foreseeable future as we seek to advance product candidates through preclinical and clinical development, expand our research and development activities, develop new product candidates, complete preclinical studies and clinical trials, seek regulatory approval and, if we receive approval from the FDA or foreign regulatory authorities, commercialize our products. Furthermore, the costs of advancing product candidates into each succeeding clinical phase tend to increase substantially over time. The total costs to advance any of our product candidates to marketing approval in even a single jurisdiction is substantial. Our prior losses, combined with expected future losses, will continue to have an adverse effect on our stockholders' deficit and working capital. We anticipate that our expenses will increase substantially if and as we:

- progress our ANTLER phase 1 clinical trial for our CB-010 product candidate;
- continue our current research programs and our preclinical and clinical development of our other current product candidates, including CB-011, CB-012, and CB-020, and any other product candidates we identify and choose to develop;
- hire additional clinical, quality control, and scientific personnel;
- seek to identify additional research programs and additional product candidates;
- further develop our genome-editing technologies;
- acquire or in-license technologies;
- expand, maintain, enforce, and defend our intellectual property estate;
- seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical trials, if any;
- establish and expand manufacturing capabilities and supply chain capacity for our product candidates;
- add operational, legal, financial, and management information systems and personnel;
- experience any delays, challenges or other issues associated with any of the above, including the failure of clinical trials meeting endpoints, the generation of unanticipated preclinical study results or clinical trial data subject to differing interpretations, or the occurrence of potential safety issues or other development or regulatory challenges;
- make royalty, milestone, or other payments under current, and any future, in-license or assignment agreements;

- establish a sales, marketing, and distribution infrastructure to commercialize any product candidates for which we obtain marketing approval; and
- continue to operate as a public company.

Because of these risks, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

We will need substantial additional financing to develop our product candidates and implement our operating plans. If we fail to obtain additional financing, we may be delayed or unable to complete the development and commercialization of our product candidates.

Despite the completion of our initial public offering ("IPO") in July and August 2021, we will continue to need additional capital beyond the IPO proceeds, which we may raise through equity offerings, debt financings, collaborations and strategic alliances, licensing arrangements, or other sources. Additional sources of financing might not be available on favorable terms, if at all. If we fail to raise additional funds on acceptable terms, we might be unable to complete the development or obtain marketing approval of any of our product candidates, and we could be forced to delay or discontinue product development and commercialization.

We expect to spend a substantial amount of capital in the research, development, and manufacture of our product candidates. We expect our expenses to increase in connection with our ongoing activities, particularly as we initiate clinical trials for, and seek marketing approval of, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that we do not obtain commercialization partners who will bear the costs for such activities. We may also need to raise additional funds sooner if we choose to pursue additional indications or markets for our product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we will continue to incur significant costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we will be forced to delay, reduce, or eliminate certain of our research and development programs or future commercialization efforts. Because our allogeneic cell therapy product candidates are based on new technologies, they require extensive research and development and have substantial manufacturing costs. In addition, clinical costs to treat cancer patients with our product candidates, including treatment of any potential side effects that may arise, will be significant.

As of December 31, 2021, we had cash, cash equivalents, and marketable securities of $413.5 million. We expect our cash, cash equivalents, and marketable securities to be sufficient to fund our current operating plan through at least the next 12 months from the date the consolidated financial statements included in this Annual Report on Form 10-K are issued. Our expectation is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- costs, progress, and results of our product candidate preclinical studies and clinical trials;
- potential delays in our preclinical studies and clinical trials, whether current or planned, due to unforeseen events as well as other factors such as the economic environment or the COVID-19 pandemic;
- costs and prioritization of our research and development programs as well as costs to acquire or in-license technologies or other product candidates;
- expansion of our workforce or our facilities;
- costs of establishing and maintaining a supply chain for the development and manufacture of our product candidates;
- timing and outcome of regulatory review of our product candidates;
- success of our collaboration with AbbVie and our receipt of reimbursements due thereunder;
- our ability to establish and maintain additional collaborations on favorable terms;
- costs of fulfilling our contractual obligations to reimburse certain parties for costs incurred in connection with the prosecution and maintenance of licensed patent rights, including reimbursements owed to The Regents of the University of California;

- achievement of milestones that trigger payments under any of our current license and assignment agreements as well as under any additional agreements we enter into in the future;
- costs of preparing, filing, prosecuting, and maintaining our patent portfolio, including costs associated with administrative proceedings of patent offices;
- litigation costs in the event we seek to enforce our patents against third parties or if we are sued for infringement by third parties;
- effects of competing technologies, success or failure of products similar to our product candidates, and market developments;
- costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our product candidates; and
- costs of operating as a public company.

Changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than expected because of circumstances beyond our control. We may also need to raise additional capital sooner if we choose to expand programs, personnel, and facilities more rapidly than planned. In any event, we will require additional capital for the further research, development, and commercialization of our product candidates, including potentially establishing our own internal manufacturing capabilities. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to research, develop, and commercialize our product candidates.

We cannot be certain that additional funding will be available when needed and on acceptable terms, or at all. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay, or discontinue one or more of our product candidate preclinical studies, clinical trials, or development and commercialization, or we may be unable to expand our operations or otherwise capitalize on our business opportunities, as desired. Any of the above could significantly harm our business, financial condition, results of operations, and prospects and cause the price of our common stock to decline.

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

Until such time, if ever, that we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, and strategic collaboration and licensing arrangements. The terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common stock to decline. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, licensing or assigning our intellectual property rights, declaring dividends, and possibly other restrictions.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders.

If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts. Alternatively, we could be required to seek collaborators for our product candidates at an earlier stage than would otherwise be desirable or on terms that are less favorable than might otherwise be available. We might need to relinquish or license on unfavorable terms our rights to our product candidates in markets where we otherwise would seek to pursue development and commercialization ourselves, or to license our intellectual property to others who could develop products that will compete with our products. Any of these actions could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We have a limited operating history, which may make it difficult to evaluate our technologies and product candidate development capabilities or to predict our future performance.

We are a clinical-stage biotechnology company formed in 2011, with no products approved for commercial sale, and we have not generated any revenues from product sales. Our operations to date have been limited to financing and staffing our company, developing our technologies, and identifying and developing our product candidates. Our prospects must be considered in light of the uncertainties, risks, expenses, and difficulties frequently encountered by companies in their early stages of operations. We have not yet demonstrated an ability to obtain marketing approval, manufacture at commercial scale, or conduct sales and marketing activities for our product candidates, which are all necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing cell therapy products. Our ability to generate product revenue or profits, which we do not expect to occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. Unless we receive approval from the FDA or other regulatory authorities for our product candidates, we will not have product revenues. We may never be able to develop or commercialize a marketable cell therapy product.

We are early in our development efforts. To date, we have only dosed patients in our first clinical trial, which is the ANTLER phase 1 clinical trial for our CB-010 product candidate. All of our programs will require clinical development, regulatory approval, manufacturing at commercial scale, distribution channels, a commercial organization, significant marketing efforts, and substantial investment before we generate any revenue from product sales. In addition, our product candidates must be approved for marketing by the FDA before we may commercialize our products in the United States and, if we wish to commercialize our products outside the United States, by foreign regulatory agencies. Furthermore, we will continue to incur costs associated with operating as a public company, including significant legal, accounting, insurance, investor relations, and other expenses.

Additionally, the rapidly evolving nature of the genome-editing and cell therapy fields may make it difficult to evaluate our technologies and product candidates as well as to predict our future performance. Our short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties, known and unknown, that are frequently experienced by early-stage companies in rapidly evolving fields. As we advance our product candidates, we must transition from a company with a research focus to a company capable of supporting clinical development and, if successful, commercial activities. We may not be successful in such transitions. If we do not address these risks successfully, our business will suffer. Similarly, we expect that our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. As a result, you should not rely upon the results of any quarterly or annual period as an indicator of future operating performance.

Risks Relating to Our Business, Government Regulation, Technology, and Industry

We are early in our development efforts and it will be many years before we commercialize a product candidate, if ever. If we are unable to advance our product candidates through clinical trials, 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 the development of our cell therapy product candidates and have focused our research and development efforts to date on various CRISPR genome-editing technologies, including our chRDNA genome-editing technology, as well as identifying our initial CAR-T cell product candidates. Our future success depends heavily on the successful development of our product candidates. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will be a result of the successful development and eventual commercialization of our product candidates, which may never occur. Our product candidates may have adverse side effects or fail to demonstrate safety and efficacy. Additionally, our product candidates may have other characteristics that may make them impractical or prohibitively expensive for large-scale manufacturing. Furthermore, our product candidates may not receive regulatory approval or, if they do, they may not be accepted by the medical community or patients or may not be competitive with other products that become available. We currently have no product revenue and we may never be able to successfully develop or commercialize a marketable product.

We must submit IND applications to the FDA to initiate clinical trials in the United States. In September 2020, we announced that the FDA had cleared our IND application for our first product candidate, CB-010. The filing of future IND applications for our other product candidates is subject to additional preclinical research, research-scale and clinical-scale manufacturing, exploration of possible other genome-editing systems, evaluation of potential targets, and other factors yet to be identified. In the case of our CB-012 product, we will need to identify and select our Cas12a chRDNA guides with acceptable accuracy and efficiency. In addition, commencing any new clinical trial is subject to review by the FDA based on the acceptability and sufficiency of our chemistry, manufacturing, and controls ("CMC"), and preclinical information provided to support our IND applications. If the FDA or foreign regulatory authorities require us to complete additional preclinical studies or we are required to satisfy other requests for additional data or information, our clinical trials may be delayed. Even after we receive and incorporate guidance from the FDA or foreign

regulatory authorities, these regulatory authorities could disagree that we have satisfied all requirements to initiate our clinical trials or they may change their position on the acceptability of our trial design or the clinical endpoints selected. They could impose a clinical hold, which may require us to complete additional preclinical studies or clinical trials. The success of our product candidates will depend on several factors, including the following:

- sufficiency of our financial and other resources;
- acceptance of our chRDNA genome-editing technology;
- ability to develop and deploy armoring technologies so that our product candidates have a competitive edge;
- completion of preclinical studies;
- clearance of IND applications to initiate clinical trials;
- successful enrollment in, and completion of, our clinical trials;
- data from our clinical trials that support an acceptable risk-benefit profile of our product candidates for our intended patient populations and indications and demonstrate safety and efficacy;
- establishment of agreements with CMOs for clinical and commercial supplies and scaling up of manufacturing processes and capabilities to support our clinical trials;
- successful development of our internal process development and transfer to larger-scale facilities;
- receipt of regulatory and marketing approvals from applicable regulatory authorities;
- receiving regulatory exclusivity for our product candidates;
- establishment, maintenance, enforcement, and defense of patent and trade secret protection and other intellectual property rights;
- not infringing, misappropriating, or otherwise violating third-party intellectual property rights;
- entry into collaborations to further the development of our product candidates or for the development of new product candidates;
- establishing sales, marketing, and distribution capabilities for commercialization of our product candidates if and when approved, whether by us or in collaboration with third parties;
- maintenance of a continued acceptable safety profile of products post-approval;
- acceptance of product candidates, if and when approved, by patients, the medical community, and third-party payors;
- effective competition with other therapies and treatment options;
- establishment and maintenance of healthcare coverage and adequate reimbursement; and
- expanding indications and patient populations for our products post-approval.

Our product candidates are cell therapies generated by novel CRISPR chRDNA genome-editing technologies, which make it difficult to predict the time and cost of developing these product candidates and obtaining regulatory approval. To date, no other products that use these genome-editing technologies have advanced into clinical trials or received marketing approval in the United States.

We are concentrating our initial research, development, and manufacturing efforts on our allogeneic CAR-T cell therapies that are intended to treat patients with certain cancers. Before obtaining regulatory approval for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex, and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for their intended use. The clinical trial requirements of the FDA and other regulatory authorities, and the criteria these regulators use to determine the safety and efficacy of a product candidate, vary substantially according to the type, complexity, novelty, intended use, and target population of our product candidates. The outcome of preclinical studies and clinical trials is inherently uncertain. Failure can occur at any time during the preclinical study and clinical trial processes

and because we have never successfully commercialized a product and our first product candidate is in an early stage of clinical development, there is a high risk of failure. We may never succeed in developing marketable products.

Approval processes by the FDA or other regulatory authorities for existing autologous anti-CD19 and anti-BCMA CAR-T cell therapies may not be indicative of what these regulatory authorities will require for approval of our allogeneic anti-CD19 CAR-T cell therapy or our other product candidates. Also, although we expect reduced variability in our allogeneic products candidates compared to autologous products, we do not have any clinical data supporting benefits of lower variability, and the use of healthy donor material may create separate variability challenges for us. Moreover, our product candidates may not perform successfully in clinical trials or may be associated with serious adverse events that distinguish them from the autologous anti-CD19 and anti-BCMA CAR-T therapies that have previously been approved. For instance, allogeneic product candidates may result in GvHD, which is not experienced with autologous products. GvHD results when allogeneic T cells see the patient's normal tissue as foreign and attack and damage those cells. Even if we collect promising initial clinical data for our product candidates, longer-term data may reveal adverse events or responses that are not durable. Negative clinical outcomes would significantly impact our business.

In addition, approved autologous CAR-T therapies and those under development have shown frequent rates of cytokine release syndrome, neurotoxicity, serious infections, prolonged cytopenia, hypogammaglobulinemia, and other serious adverse events that have resulted in patient death. There may be similar adverse events for our allogeneic CAR-T and CAR-NK cell therapy product candidates, including patient death. Moreover, patients eligible for allogeneic CAR-T cell therapies but ineligible for autologous CAR-T cell therapies due to aggressive cancer or an inability to wait for autologous CAR-T cell therapies may be at greater risk for complications and death from therapy. Our allogeneic CAR-T cell product candidates may also cause unique adverse events related to the differences between the donor and patients, such as GvHD or infusion reactions. Our product candidates may not be successful in limiting the risk of GvHD, exhaustion of the CAR-T cells, or premature rejection by a patient's immune system. If significant GvHD or other serious adverse events are observed with the administration of our product candidates, or if any of our product candidates are viewed as less safe or effective than autologous therapies or other allogeneic therapies, our ability to develop other allogeneic therapies may be adversely affected.

We use our CRISPR chRDNA genome-editing platform to generate our product candidates, and we believe our chRDNA guides significantly improve the specificity of CRISPR genome editing (e.g., by reducing the number of off-target events). CRISPR genome editing generally is relatively new; to date, no genome-editing technologies have been approved in the United States although clinical trials of product candidates based on CRISPR-Cas9 and other genome-editing technologies are underway. As a result, the regulatory approval process for cell therapy product candidates such as ours is uncertain and may be more expensive and take longer than the approval process for product candidates based on better known or more extensively studied technologies. As such, it is difficult to accurately predict the developmental challenges we may face as we progress our product candidates through preclinical studies and clinical trials. There may be long-term adverse effects from treatment with our product candidates resulting from the use of our chRDNA genome-editing technology that we cannot predict with the knowledge we have today. Also, animal models may not exist for some of the diseases we choose to pursue in our programs, which may complicate and increase the cost of preclinical research. As a result of these factors, it is difficult for us to predict the time and cost of our product candidate development, and we cannot predict whether the application of our chRDNA genome-editing technology, or other genome-editing technologies we may use in the future, will result in the identification, development, preclinical studies, and clinical trials to support regulatory approval of any of our cell therapy product candidates. There can be no assurance that any development problems we experience in the future related to our chRDNA genome-editing technology or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may not achieve the desired safety and efficacy of our product candidates. Also, we may not sufficiently improve genome-editing specificity and our genome editing may have off-target events. Moreover, we may not be able to achieve a high degree of on-target gene knockout and insertion efficiency in developing our product candidates. Although we plan to disclose initial clinical data from the ANTLER clinical trial for our CB-010 product candidate in 2022, any of these factors may prevent us from completing our clinical trials, delay or cause us to fail to meet our clinical trial endpoints, or lead us to fail to commercialize any of our cell therapy product candidates.

We may also experience delays in developing robust, reproducible, and scalable manufacturing processes and transferring those processes to CMOs, which may prevent us from completing our clinical trials or commercializing our products on a timely or profitable basis, if at all. Currently, we have only manufactured our CB-010 product candidate for clinical trials. In addition, since we are in the early stages of clinical development, we do not know the doses to be used in later phase 2 or pivotal trials needed to evaluate the efficacy of our product candidates, which will affect the manufacturing requirements for our product candidates. Finding a suitable dose, such as a maximum tolerated dose or, as applicable, a recommended phase 2 dose, for our cell therapy product candidates may delay our anticipated clinical development timelines and prolong our clinical trials. Accordingly, our expectations regarding our costs of manufacturing may vary significantly as we develop our product candidates and understand these critical factors. Such factors may delay or keep us from bringing a product candidate to market and could decrease our ability to generate sufficient product revenue, which could harm our business, financial condition, results of operations, and prospects.

Manufacturing of our product candidates is complex and we could experience manufacturing problems during our clinical trials, which could delay or limit commercialization of our product candidates.

The manufacturing processes used to produce our cell therapy product candidates are and will be complex, as our product candidates are novel products and, to date, only our CB-010 product candidate has been manufactured according to cGMPs. Several factors could cause production interruptions including facility contaminations; shortages or quality problems; contamination of healthy donor cells, chRDNA guides, Cas proteins, viruses, iPSC master cell banks or working cell banks; natural disasters, including the COVID-19 pandemic; labor shortages and strikes; lack of experienced scientific, quality control, and manufacturing personnel; human error; or other disruptions in the operations of our suppliers and CMOs. We conduct process development activities at our facilities and we may experience personnel and supply shortages. Problems with our manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims, or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical grade materials that meet FDA or other applicable standards or specifications with consistent and acceptable production yields and costs.

As our product candidates proceed through preclinical studies to clinical trials to regulatory review, and potential marketing approval and commercialization, it is common that various aspects of our manufacturing methods will be altered along the way to optimize processes and results. Such changes carry the risk that intended objectives will not be achieved. If we make any such changes, our product candidates could perform differently and affect the results of clinical trials conducted with the altered materials. Such changes may also require additional testing as well as notification to or approval from the FDA or other regulatory authorities, which could delay completion of our clinical trials, require bridging clinical trials, require repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates, if any, and ultimately jeopardize commercialization.

If we receive marketing approval for a product candidate, the FDA and other regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA or other 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. Problems in our manufacturing processes could restrict our ability to meet market demand for our products. All these factors could be costly to us and otherwise harm our business, financial condition, results of operations, and prospects.

Our business is highly dependent on the success of our product candidates, which will require significant additional preclinical studies and and/or human clinical trials before we can seek regulatory approval and potentially commercialize our product candidates. If we are unable to advance our preclinical studies and clinical trials and obtain regulatory approval for, and successfully commercialize, our lead product candidates for the treatment of patients in approved indications, or if we are significantly delayed in doing so, our business will be significantly harmed.

Our business and future success depends on our ability to advance our product candidates through preclinical studies and clinical trials, obtain regulatory approval for, and successfully commercialize, our product candidates. Because CB-010 is our first allogeneic cell therapy product to be evaluated in the clinic, the failure of our lead product candidate, or the failure of other companies' allogeneic anti-CD19 CAR-T cell therapies, including for reasons due to safety, efficacy, or durability, may impede our ability to develop not only CB-010 but our other CAR-T and CAR-NK product candidates as well, and may significantly influence physicians' and regulatory authorities' opinions with regard to the viability of our entire pipeline of allogeneic cell therapies. In order to submit IND applications for our other product candidates, we will need to complete many objectives, such as our preclinical research of product candidates still in discovery and advancement of cGMP conditions for our product candidates. If we are unable to achieve any of these objectives, we may not be able to submit other IND applications in a timely manner or at all, which would significantly harm our business.

We may not be successful in our efforts to identify and successfully research and develop additional product candidates and may expend our limited resources to pursue particular product candidates or indications while failing to capitalize on other product candidates or indications that may be more profitable, or for which there is a greater likelihood of commercial success.

Part of our business strategy involves identifying and developing new cell therapy product candidates. The process by which we identify product candidates may fail to yield successful product candidates for a number of reasons, including:

- we may not be able to assemble sufficient resources to identify or acquire additional product candidates;
- competitors may develop alternative therapies that render new product candidates obsolete or less attractive;

- product candidates we develop or acquire may be covered by third-party intellectual property rights;
- new product candidates may, on further study, be shown to have adverse side effects, toxicities, or other characteristics that indicate that they are unlikely to receive marketing approval or achieve market acceptance;
- new product candidates may not be safe or effective;
- the market for a new product candidate may change so that the continued development of that product candidate is no longer reasonable; and
- we may not be able to produce new product candidates in commercial quantities at an acceptable cost, or at all.

We have limited financial and managerial resources. We are focused initially on allogeneic CAR-T and CAR-NK cell therapies and, as a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing, or other royalty arrangements when it would have been more advantageous for us to retain sole development and commercialization rights to that product candidate.

If we experience delays or difficulties enrolling patients in the clinical trials for our product candidates, including our ANTLER phase 1 clinical trial for our CB-010 product candidate, our ability to advance our lead and other product candidates through clinical development and the regulatory process could be delayed or prevented.

The timely completion of clinical trials depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may encounter delays in enrolling or be unable to enroll a sufficient number of patients to complete any of our clinical trials and, even if patients are enrolled, they may withdraw from our clinical trials before completion. For our ANTLER phase 1 clinical trial, we have entered into a contract with a clinical research organization ("CRO"), as well as clinical trial agreements with the sites participating in our clinical trial. Patient selection and enrollment may be challenging. Our clinical protocol excludes many non-Hodgkin lymphoma patients from the ANTLER phase 1 clinical trial, including patients previously treated with anti-CD19-targeted therapy or allogeneic stem cell transplantation, patients with active or chronic GvHD requiring therapy, or patients unwilling to follow extended safety monitoring.

Our ANTLER phase 1 clinical trial, as well as any future clinical trials for our other product candidates, will compete for enrollment of patients with other clinical trials for product candidates that are in the same cell therapeutic areas with the same or similar study populations as our product candidates. Our clinical trials will also compete for enrollment of patients with other clinical trials for product candidates based on non-cellular modalities, such as small molecules and antibodies, that are intended for the same or similar study populations as our product candidates. This competition will reduce the number and types of patients available to us because some patients who might opt to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Additionally, since the number of qualified and experienced clinical investigators for therapeutic areas is limited, some of our clinical trial sites may be also conducting clinical trials for some of our competitors, which may reduce the number of patients who are available for our clinical trials at that clinical trial site. 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, hematopoietic stem cell transplantation, or autologous CAR-T cell therapies, rather than refer patients to our clinical trials. Because our cell therapy product candidates are edited with CRISPR chRDNA guides, our products may be perceived to have additional or greater safety risks. Patients eligible for allogeneic CAR-T cell therapies but ineligible for autologous CAR-T cell therapies may be difficult to treat due to advanced and aggressive cancers and may fail to experience improved outcomes and be at greater risk for complications and death from our product candidates. If patients are unwilling to participate in our cell therapy trials, the timeline for recruiting patients, conducting clinical trials, and obtaining regulatory approval of any of our product candidates may be delayed.

In addition, the enrollment of patients depends on many factors, including:

- severity or stage of the type of cancer under investigation;
- size of the patient population and process for identifying patients;
- design of the clinical trial protocol;

- regulatory hold on clinical trial recruitment because of unexpected safety events;
- availability of eligible prospective patients who are otherwise eligible patients for competitive clinical trials;
- availability and efficacy of approved alternative treatments for the disease under investigation;
- ability to obtain and maintain patient consent;
- risk that enrolled patients will drop out before completion of the trial;
- eligibility and exclusion criteria for the trial in question;
- perceived risks and benefits of our product candidates;
- perceived risks and benefits of genome-editing and cell therapies;
- perceived risks and benefits of participating in a clinical trial;
- efforts by clinical sites and investigators to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- physicians' ability to monitor patients adequately during and after treatment because of patient healthcare access issues caused by COVID-19, other pandemics, or public health crises;
- proximity and availability of clinical trial sites for prospective patients; and
- interruptions, delays, or staffing shortages resulting from the COVID-19 pandemic, other pandemics, or public health crises.

Enrollment delays in our clinical trials may result in increased development costs for any product candidates we may develop, which may cause our stock price to decline and limit our ability to obtain additional financing. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit, or terminate our ANTLER phase 1 clinical trial or future clinical trials, and postpone or forgo seeking marketing approval, any of which would have an adverse effect on our business, financial condition, results of operations, and prospects.

Clinical trials are expensive, time consuming, and subject to uncertainty. We cannot guarantee that any of our clinical trials will be conducted as planned or completed on schedule, if at all. Issues may arise that could suspend or terminate our clinical trials. A failure of one or more of our clinical trials may occur at any stage of testing, and our future clinical trials may not be successful.

Events that may prevent successful or timely completion of clinical development include:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;
- delays or failure to obtain regulatory clearance to initiate our clinical trials, as well as delays or failures to obtain any necessary approvals by the clinical sites;
- delays, suspension, or termination of our clinical trials by the clinical sites;
- modification of clinical trial protocols;
- delays in 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, as well as possible future breaches of such agreements;
- failure to manufacture sufficient quantities of our product candidates for use in our clinical trials;
- failure by third-party suppliers, CMOs, CROs, and clinical trial sites to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- imposition of a temporary or permanent clinical hold by us, IRBs for the institutions at which such trials are being conducted, or by the FDA or other regulatory authorities for safety or other reasons, such as a result of a new safety finding in a clinical trial on a similar product by one of our competitors, that presents unreasonable risk to clinical trial participants;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which we developed our clinical development plan, which may require new or additional trials;
- the cost of clinical trials of our product candidates being greater than we anticipated;
- insufficient funding to continue clinical trials with our product candidates;
- the emergence of unforeseen safety issues or undesirable side effects;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of our product candidates;
- inability to establish clinical trial endpoints that applicable regulatory authorities consider clinically meaningful, or, if we seek accelerated approval, that applicable regulatory authorities consider likely to predict clinical benefit;
- regulators withdrawing their approval of a product or imposing restrictions on its distribution; and
- interruptions, delays, or staffing shortages resulting from the COVID-19 pandemic, other pandemics, or public health crises.

If (i) we are required to extend the duration of any clinical trials or to conduct additional preclinical studies or clinical trials or other testing of our product candidates beyond those that we currently contemplate; (ii) we are unable to successfully complete preclinical studies or clinical trials of our product candidates or other testing; (iii) the results of these trials, studies, or tests are negative or produce inconclusive results; (iv) there are safety concerns; or (v) we determine that the observed safety or efficacy profile would not be competitive in the marketplace, we may:

- abandon the development of one or more product candidates;
- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all;
- obtain marketing approval in some jurisdictions and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as we intended or designed;
- obtain marketing approval with labeling that includes significant use restrictions or safety warnings, including black box warnings;
- be subject to additional post-marketing requirements; or
- have regulatory agencies remove the product from the market or we voluntarily withdraw the product from the market after obtaining marketing approval.

Our clinical trials may fail to adequately demonstrate the safety and efficacy of any of our product candidates and the development of our product candidates may be delayed or unsuccessful, which could prevent or delay regulatory approval and commercialization.

Our product candidates are in various stages of preclinical and clinical development. If we encounter safety or efficacy problems in our ongoing or future studies, our developmental plans and business could be significantly harmed. Product candidates in later stages of clinical trials may fail to show the desired safety profiles and efficacy results despite having progressed through initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Based upon negative or inconclusive results, we may decide, or regulatory agencies may require us, to conduct additional clinical trials or preclinical studies.

In addition, data obtained from clinical trials are susceptible to varying interpretations, and regulatory agencies may not interpret our data as favorably as we do, which may delay, limit, or prevent regulatory approval.

In addition, the design of a clinical trial can determine whether its results will support approval of our product candidates, and flaws in the design of a clinical trial may not be apparent until the clinical trial is well advanced. We have limited experience designing clinical trials and may be unable to design and execute a clinical trial that will support regulatory approval.

From time to time, we may publish initial, interim, or preliminary data from our clinical trials. Initial, interim, or preliminary data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully evaluate all data at the time of publishing initial, interim, or preliminary data. These data also remain subject to audit and verification procedures that may result in the final data being materially different from the data we previously published. As a result, initial, interim, and preliminary data should be viewed with caution until the final data are available. Moreover, initial, interim, and preliminary data are subject to the risk that one or more of the clinical outcomes may materially change as more patient data become available when patients mature on study, patient enrollment continues, or, for final data, as other ongoing or future clinical trials with a product candidate further develop. Past results of clinical trials may not be predictive of future results. Unfavorable differences between initial, interim, or preliminary data and final data could significantly harm our business prospects and may cause the trading price of our common stock to decline significantly.

Because of these risks, our product candidates may fail or encounter difficulties in clinical trials. If we are unable to advance our product candidates through clinical trials to seek marketing approval, our business, financial condition, results of operations, and prospects will be materially harmed.

If our product candidates cause serious adverse events or undesirable side effects, including injury and death, or have other properties that could delay or prevent regulatory approval, their commercial potential may be limited or extinguished.

Product candidates we develop may be associated with undesirable or unacceptable side effects, unexpected characteristics, or other serious adverse events, including death. Immunotherapy, and its method of action of harnessing the immune system, is powerful and could lead to serious side effects that we only discover in clinical trials. In addition to potential serious adverse events from the immune system or side effects caused by our CB-010 product, or any product candidate we may develop and advance into one or more clinical trials, the product candidate administration process and related procedures may also cause undesirable side effects. Patients who enroll in our ANTLER phase 1 clinical trial, and future clinical trials, will undergo a lymphodepletion regimen, including administration of fludarabine and cyclophosphamide, which can lead to serious adverse events. Because these regimens will cause a transient and sometimes prolonged blood count suppression, patients will have an increased risk of leukopenia, anemia, thrombocytopenia bleeding, or infection, which could ultimately lead to death. We expect to educate clinical site personnel administering our cell therapy product candidates to understand the side effect profiles for our product candidates. Inadequate recognition or management of the potential side effects of our product candidates could result in patient injury or death. If any undesirable or unacceptable side effects, unexpected characteristics, or other serious adverse events occur, our clinical trials could be suspended or terminated, and our business and reputation could suffer substantial harm.

There can be no assurance that we will resolve any adverse event related to any of our products to the satisfaction of the FDA or any regulatory agency in a timely manner or at all. If in the future we are unable to demonstrate that such adverse events were caused by factors other than our product candidates, the FDA or other regulatory authorities could order us to cease further clinical trials of, or deny approval of, our product candidates. Even if we demonstrate that such serious adverse events are not product candidate-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete our clinical trials. Moreover, if we elect, or are required, to delay, suspend, or terminate any clinical trial of any of our product candidates, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from these product candidates may be delayed or eliminated. Any of these occurrences may harm our business, financial condition, results of operations, and prospects.

The FDA or other regulatory agencies may disagree with our regulatory plans and we may fail to obtain regulatory approval of our cell therapy product candidates.

If and when our ANTLER phase 1 clinical trial for our CB-010 product candidate is completed and, assuming positive data, we will propose to advance to a pivotal clinical trial. Although the FDA has found substantial evidence to support approval outside of the traditional phase 1, phase 2, and phase 3 framework for the approved autologous anti-CD19 and anti-BCMA CAR-T cell therapies, the general approach for FDA approval of a new biologic is for the sponsor to provide dispositive data from at least two adequate and well-controlled clinical trials of the relevant biologic in the applicable patient population. Such clinical trials typically involve hundreds of patients, have significant costs, and take years to complete. We do not have agreement or guidance from the FDA that our

regulatory development plans will be sufficient for submission of a BLA. For example, the FDA may require that we conduct a comparative trial against an approved therapy, such as an approved autologous CAR-T cell therapy, which would significantly delay our development timelines and require substantially more resources. In addition, the FDA may limit our evaluation to patients who have failed or who are ineligible for autologous therapy, patients who may be difficult to treat, or patients with advanced and aggressive cancer, and our product candidates may fail to improve outcomes for those patients.

In addition, the standard of care may change with the approval of new products in the same indications to which our cell therapy product candidates are directed. This may result in the FDA or other regulatory authorities requesting additional studies to show that our product candidate is comparable or superior to the new products.

Our clinical trial results may also not support marketing approval. In addition, our product candidates could fail to receive regulatory approval for many reasons, including:

- the FDA or other regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that our product candidates are safe and effective for their proposed indications;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or other regulatory authorities for approval, including due to heterogeneity of patient populations;
- we may be unable to demonstrate that the clinical and other benefits of our product candidates outweigh the safety risks;
- the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the FDA or other regulatory authorities to support the submission of a BLA or a similar filing in a foreign jurisdiction or to support commercial reimbursement;
- the FDA or other authorities will review our manufacturing processes and inspect our CMOs' facilities and may not approve our manufacturing processes or CMOs' facilities; and
- the approval policies or regulations of the FDA or other regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Even if we comply with all FDA requests, we may still fail to obtain regulatory approval. We cannot be sure that we will ever obtain regulatory clearance for our product candidates. Failure to obtain FDA approval of our product candidates will severely undermine our business by leaving us without a commercially marketable product in the United States, and therefore without any source of revenues from product sales in the United States, until another product candidate can be developed or obtained and ultimately approved.

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time-consuming, and uncertain, and we may be unable to obtain the regulatory approvals necessary for the commercialization of our product candidates; furthermore, if there are delays in obtaining regulatory approvals, we may not be able to commercialize our products, may lose competitive lead time, and our ability to generate revenues will be materially impaired.

The process of obtaining marketing approvals, both in the United States and in other jurisdictions, is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. It is impossible to predict if or when any of our product candidates will prove to be safe and effective in humans or if we will receive regulatory approval for such product candidates. The risk of failure through the development process is high. Any product candidates we may develop, and the activities associated with their development and commercialization, including their manufacture, preclinical and clinical development, safety, efficacy, recordkeeping, labeling, storage, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities.

Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval or authorization to market any product candidates from regulatory authorities in any jurisdiction and it is possible that none of our product candidates or any product candidates we may seek to develop in the future will ever obtain marketing approval or commercialization. We have not previously submitted a BLA to the FDA or made a similar submission to any foreign regulatory authority. A BLA must include extensive preclinical and clinical data and supporting information to establish our product candidate's safety and efficacy for each desired indication. The BLA must also include significant information regarding the chemistry, manufacturing, and controls for our product. Any product candidates we develop may not be effective; may

be only moderately effective; or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. The FDA and other regulatory authorities have substantial discretion in the approval process and may refuse to accept our BLA applications and decide that our data are insufficient and require additional preclinical studies or clinical trials. The same may happen with review of our product candidates by foreign regulatory authorities. In addition, varying interpretations of the data obtained from preclinical studies and clinical trials could delay, limit, or prevent marketing approval of our product candidates. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render our approved product not commercially viable. If we experience delays in obtaining approval or if we fail to obtain approval of any product candidates we may develop, the commercial prospects for those product candidates and our ability to generate revenues will be materially impaired and we may lose competitive lead time as similar products enter the market.

We expect the novel nature of our product candidates to create further challenges in obtaining regulatory approval. For example, the FDA has limited experience with the development of allogeneic T cell and NK cell therapies for cancer. We may also request regulatory approval of future CAR-T or CAR-NK cell therapy product candidates by target, regardless of cancer type or origin, which the FDA may have difficulty accepting if our clinical trials have only involved cancers of certain types or origins. The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data. The opinion of an Advisory Committee, although not binding, may have a significant impact on our ability to obtain marketing approval of our product candidates based on our completed clinical trials, as the FDA often adheres to an Advisory Committee's recommendations. Accordingly, the regulatory approval pathway for our product candidates may be uncertain, complex, expensive, and lengthy, and approval may not be obtained.

The regulatory landscape that will govern our product candidates is uncertain; regulations relating to more established gene therapy and cell therapy products are still developing, and changes in regulatory requirements could result in delays or discontinuation of development of our product candidates or unexpected costs in obtaining regulatory approval.

Because we are developing novel CAR-T and CAR-NK cell therapy product candidates that are unique biological entities, the regulatory requirements to which we will be subject are not entirely clear. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. For example, regulatory requirements governing gene therapy products and cell therapy products have changed frequently and may continue to change in the future. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. Gene therapy clinical trials are also subject to additional review and oversight by an IBC. Although the FDA decides whether individual gene therapy protocols may proceed, review processes and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the study and cleared its initiation. Conversely, the FDA can place an IND application on clinical hold even if such other entities have provided a favorable review.

We may apply for Regenerative Medicine Advanced Therapy designation, Breakthrough Therapy Designation, and Fast Track Designation review by the FDA for some, if not all, of our allogeneic CAR-T and CAR-NK cell therapies, but there are no assurances that we will receive any of these designations or that the FDA will grant priority review to any of our product candidates.

We may apply for certain expedited programs in the United States, such as RMAT, breakthrough therapy, fast track, or priority review programs. Although obtaining each of these designations has specific and different criteria, they are reserved for therapeutic products that are intended for serious diseases, and each designation offers certain benefits to prioritize the review and approval of such therapeutic option, which may include rolling reviews, intensive guidance, or approval based on surrogate endpoint or an intermediate clinical endpoint that is reasonably likely to predict a drug's clinical benefit. However, there is no assurance that we will be able to obtain such a designation, if any, for any of our product candidates. Even if we obtain an expedited designation, we may ultimately fail to obtain FDA's full approval for our product candidates, or the approved indication may be narrower than the indication covered by the designation.

We may seek orphan drug designation for some or all of our allogeneic CAR-T and CAR-NK cell therapy product candidates across various indications, but we may not be able to obtain such designations or to maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our revenue, if any, to be reduced.

We plan to submit applications to FDA for orphan drug designation for some or all our allogeneic CAR-T and CAR-NK cell therapy product candidates in specific orphan indications in which there is a medically plausible basis for the use of these products. There is no guarantee that we will obtain such a designation, and the FDA may decline our request if it determines that our product candidates and the proposed indications do not meet the threshold for the orphan drug designation. Even if we obtain orphan drug designation, we may not be the first company to obtain FDA approval for the orphan drug indication, in which case exclusive marketing rights would not be available to us. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request

for designation was materially defective, we are unable to ensure sufficient quantities of the product to meet the needs of patients with the rare disease or condition, or if a subsequent applicant demonstrates clinical superiority over our products.

Our allogeneic CAR-T and CAR-NK cell therapy product candidates will be regulated as biological products, or biologics, and therefore may be subject to uncertainty regarding regulatory exclusivity or maintaining regulatory approval.

Under the BPCIA, the FDA has the authority to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic. An application for a biosimilar product cannot be approved by the FDA until 12 years after the reference product was approved under a BLA. We believe that our product candidates should qualify for the 12-year period of exclusivity. However, some uncertainty over interpretation of the law remains, and there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for drug products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

Even if we obtain marketing approvals for our product candidates, the terms of such approvals and ongoing regulation of our products could require substantial expenditure of resources and may limit how we manufacture and market our products, which could materially impair our ability to generate revenues. Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Even if we receive marketing approval for a product candidate, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval or contain requirements for costly post-marketing testing and studies to further assess the safety or efficacy of the product. The FDA also may place other conditions on our approval, including the requirement for a REMS to ensure the safe use of the product by reinforcing medication use behaviors and actions. If the FDA concludes a REMS is needed, we must submit a proposed REMS before our product candidate will be eligible to receive marketing approval. A REMS could include medication guides, physician communication plans, or other elements to ensure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. Certain REMS programs can significantly impact and restrict the marketability of our products, even if our products are approved.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates. If we are slow to address 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, which would adversely affect our business, prospects, and ability to achieve or sustain profitability. Any government investigation of alleged violations of law, including investigations of any of our suppliers or CMOs, could require us to expend significant time and resources in response and could generate negative publicity. Accordingly, we will need to continue to expend time, money, and effort on regulatory compliance activities. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approval for our products withdrawn by regulatory authorities and our ability to market any product candidates could be limited, which could adversely affect our ability to achieve or sustain profitability. Furthermore, the cost of compliance with post-approval regulations, including REMS, may have a negative effect on our business, financial condition, results of operations, and prospects.

The FDA and other regulatory authorities closely regulate the post-approval marketing and promotion of biologics to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory authorities impose stringent restrictions on off-label promotion, and if we market our products for unapproved indications, including off-label indications, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the DOJ. Violation of the FDCA and other statutes, including the federal False Claims Act, relating to the promotion and advertising of prescription products, may also lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown problems with our products or the manufacturing of our products, may cause:

- restrictions on our products or the manufacturing of our products;
- restrictions on the labeling or marketing of our products;
- restrictions on the exportation, distribution, or use of our products;
- requirements to conduct post-marketing clinical trials;

- receipt of warning or untitled letters;
- withdrawal of our products from the market;
- refusal to approve pending BLAs or BLA supplements that we submit;
- recall of our products;
- fines, restitution, or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- suspension of any ongoing clinical trials;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

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

We may never obtain approval to commercialize our product candidates outside the United States, which could limit our ability to recognize the full market potential of our product candidates and could materially impair our ability to generate revenues.

In order to market and sell any of our product candidates in the EU or other foreign jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and jurisdictions and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all the risks associated with obtaining FDA approval. In addition, in many countries, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other jurisdictions. The failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our product candidates in multiple jurisdictions, which could materially impair our ability to generate revenue.

Following the United Kingdom's exit from the EU in 2020 (commonly referred to as "Brexit"), the EU and United Kingdom entered into the EU-UK Trade and Cooperation Agreement, which was entered into force permanently on May 1, 2021. The agreement provides details on how some aspects of the United Kingdom and the EU's relationship regarding pharmaceutical products will operate; however, there are still many uncertainties. Since the regulatory framework in the United Kingdom covering pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory requirements for product candidates and products in the United Kingdom as there is now potential for the UK regulations to diverge from the EU regulations. In the meantime, the Medicines and Healthcare products Regulatory Agency (the "MHRA"), the medicines and medical devices regulator in the United Kingdom, has published detailed guidance for industry and organizations to follow as of January 1, 2021, which is updated as necessary. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could harm our business.

Negative public opinion and increased regulatory scrutiny of genetic research and therapies involving genome editing may damage public perception of our product candidates generated through genome editing or adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

The CRISPR chRDNA genome-editing technologies that we use are novel. Public perception may be influenced by claims that genome editing is unsafe, and therapeutic products generated through genome editing may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in our targeted diseases prescribing our product candidates, if approved for marketing, as treatments in lieu of, or in addition to, existing, more familiar treatments for which greater clinical data may be available. Any increase in negative perceptions of genome editing may result in fewer physicians prescribing our treatments or may reduce the willingness of patients to accept our products. In addition, given the novel nature of genome-edited and CAR-T and CAR-NK cell therapies, governments may place import, export, or other restrictions in order to retain

control or limit the use of such technologies. Increased negative public opinion or more restrictive government regulations, either in the United States or internationally, could have a negative effect on our business or financial condition and may delay or impair the commercialization of our product candidates or demand for such products.

In particular, genome-editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the potential application of genome-editing technology to human embryos or the human germline. We do not apply genome-editing technologies to human embryos or the human germline. In April 2016, a group of scientists reported on their attempts to edit the genome of human embryos to modify the gene for hemoglobin beta. This is the gene in which a mutation occurs in patients with the inherited blood disorder beta thalassemia. Although this research was purposefully conducted in embryos that were not viable, the work prompted calls for a moratorium or other types of restrictions on genome editing of human eggs, sperm, and embryos. Additionally, in November 2018, He Jiankui, Ph.D., a biophysics researcher who was an associate professor in the Department of Biology of the Southern University of Science and Technology in Shenzhen, China, reportedly claimed he had created the first human genome-edited babies, twin girls. This claim, and another that Dr. He had helped create a second genome-edited pregnancy, was subsequently confirmed by Chinese authorities and was negatively received by the public, in particular by those in the scientific community. News reports indicate that Dr. He was sentenced to three years in prison and reportedly fined $430,000 in December 2019 by the Chinese government for illegal medical practice in connection with such activities. In the wake of the claim, the World Health Organization established a new advisory committee to create global governance and oversight standards for human genome editing. The Alliance for Regenerative Medicine in Washington, D.C., of which we are a member, has called for a voluntary moratorium on the use of genome-editing technologies, including CRISPR, in research that involves altering human embryos or human germline cells and has also released a bioethical framework of principles for the use of genome editing in therapeutic applications endorsed by a number of companies that use genome-editing technologies. Similarly, the NIH has announced that it would not fund any use of genome-editing technologies in human embryos, noting that there are multiple existing legislative and regulatory prohibitions against such work, including the Dickey-Wicker Amendment, which prohibits the use of appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed.

Although we do not use our CRISPR chRDNA genome-editing technologies to edit human embryos or the human germline, such public debate about the use of genome-editing technologies in human embryos and heightened regulatory scrutiny could prevent or delay our development of our product candidates and, if approved, the market acceptance of our products. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition. Adverse events in our clinical trials or those of our competitors or of academic researchers utilizing genome-editing technologies, even if not ultimately attributable to product candidates we may identify and develop, and the resulting publicity, could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved, and a decrease in demand for any such product candidates.

We currently have no marketing and sales organization and as a company 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, we may not be able to generate product revenue.

To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must develop and build a sales and marketing team or make arrangements with third parties to perform these services. There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay our product launch. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train, and retain marketing and sales personnel. If the commercial launch of our product for which we have recruited a sales force and established marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses, which may be costly and our investment will be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, hire, train, and retain adequate numbers of effective sales, marketing, customer service, medical affairs, and other support personnel;
- our inability to equip sales personnel with effective materials, including sales literature, to help them educate physicians and other healthcare providers regarding our product candidates and their approved indications;
- our inability to effectively manage a geographically dispersed sales and marketing team;
- the inability of medical affairs personnel to negotiate arrangements for reimbursement and other acceptance by payors;

- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable or decide not to establish internal sales, marketing, and distribution capabilities, we will need to enter into arrangements with third parties to perform sales, marketing, and distribution services. In such cases, our product revenue or the profitability to us from these revenue streams is likely to be lower than if we were to market and sell any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over those third parties and they may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we may not be successful in commercializing our product candidates, and our business, financial condition, results of operations, and prospects will be materially adversely affected.

Our products may not gain market acceptance among physicians, patients, hospitals, cancer treatment centers, and others in the medical community.

The use of CAR-T and CAR-NK cells as potential cancer treatments is a recent development and may not become broadly accepted by physicians, patients, hospitals, cancer treatment centers, and others in the medical community. Ethical, social, and legal concerns about genome editing could result in the development of additional regulations restricting or prohibiting our products. Even with the requisite approvals from the FDA and other regulatory authorities internationally, the commercial success of our product candidates will depend, in significant part, on the acceptance of physicians, patients, and healthcare payors of products generated through genome editing in general, and our allogeneic CAR-T and CAR-NK cell therapy product candidates in particular, as medically necessary, cost-effective, safe, and effective therapies. We expect physicians in the large bone marrow transplant centers to be particularly important to the market acceptance of our CB-010, CB-011, and CB-012 product candidates and we may not be able to adequately educate them on the benefits and risks associated with the use of our product candidates to address concerns and foster acceptance, for many reasons. For example, certain of the product candidates that we may develop target a cell surface marker that may be present on cancer cells as well as non-cancerous cells. It is possible that our product candidates may kill these non-cancerous cells, which may result in unacceptable side effects, including death.

Additional factors will influence whether our product candidates are accepted in the market, including:

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

If our product candidates are approved 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. Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new cell therapy products,

genome-editing technologies, or other therapeutic approaches are introduced that are more favorably received than our products, are more cost effective, or render our products obsolete.

The market opportunities for our product candidates may be smaller than we currently believe and limited to those patients who are ineligible for or have failed prior treatment, which may adversely affect our business. Because the target patient populations of our product candidates are small, we must be able to successfully identify patients and capture a significant market share to achieve profitability and growth.

Our projections of both the number of patients who have the cancers we are targeting, as well as the subset of patients with these cancers in a position to receive second or later lines of therapy and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. New studies may change the estimated incidence or prevalence of these cancers. The number of eligible patients may turn out to be lower than we expected. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates. Given the small number of patients who have the eligibility criteria and diseases that we are targeting, it is critical to our ability to become profitable that we successfully identify such patients. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our business, financial condition, results of operations, and prospects. Even if we obtain significant market share for our product candidates, because the potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications.

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

The regulations that govern marketing approvals, pricing, and reimbursement for new biologic products vary widely from country to country. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some non-U.S. markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial marketing approval is granted. As a result, we might obtain marketing approval for our product candidates in a particular country, but then be subject to price regulations that delay our commercial launch of such product candidates, possibly for lengthy time periods, and such delays would negatively impact the revenues we are able to generate from the sale of our product candidates in that country. Pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Because our product candidates represent new approaches to the treatment of cancer, we cannot accurately estimate the potential revenue from our product candidates. Significant uncertainty exists as to the coverage and reimbursement status of any of our products for which we obtain regulatory approval. Additionally, reimbursement coverage may be more limited than the indications for which our products are approved. The marketability of our products may suffer if government and other third-party payors fail to provide coverage and adequate reimbursement. Furthermore, 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 of our product candidates for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Moreover, eligibility for reimbursement does not imply that our product candidates will be paid for in all cases or at a rate that will cover our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new products, 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 our product candidate and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products, and may be incorporated into existing payments for other services. Net prices for our product candidates 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 products from countries where our product candidates may be sold at lower prices than in the United States.

Third-party payors, whether domestic or foreign, 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 healthcare systems that could impact our ability to sell our product candidates, if approved, profitably. There have been, and likely will continue to be, legislative and regulatory proposals at the federal and state levels directed at broadening the availability of, and containing or lowering the cost of, healthcare. The implementation of cost containment measures that third-party payors and healthcare providers are instituting and any other healthcare reforms may prevent us from being able to generate, or may reduce, our revenues from the sale of our product candidates, if approved, and our product candidates may not be profitable. Such reforms could have an adverse effect on anticipated revenue from product candidates for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates. Even if our product candidates are successful in clinical trials and receive marketing approval, we cannot provide any assurances that we will be able to obtain and maintain third-party payor coverage or adequate reimbursement for our product candidates in whole or in part.

Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain approval of and commercialize our product candidates and could adversely affect our business.

The Affordable Care Act brought significant changes to the way healthcare is financed by both the government and private insurers, and significantly impacted the U.S. pharmaceutical industry, including expanding the list of covered entities eligible to participate in the 340B drug pricing program and establishing a new Medicare Part D coverage gap discount program. We expect that these and other healthcare reform measures in the future, may result in more rigorous coverage criteria and lower reimbursement, and in addition, exert downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may hinder us in generating revenue, attaining profitability, or commercializing our cell therapy products once, and if, marketing approval is obtained.

In the EU, coverage and reimbursement status of any product candidates for which we obtain regulatory approval are provided for by the national laws of EU member states. The requirements may differ across the EU member states. In markets outside the United States and the EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings or other price controls on specific products and therapies.

We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU, or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or those third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that we may have obtained and we may not achieve or sustain profitability.

We face significant competition from other biotechnology and pharmaceutical companies, which may result in other companies developing or commercializing products before, or more successfully than, we do, thus rendering our product candidates non-competitive or reducing the size of our market. Our operating results will suffer if we fail to compete effectively.

The biopharmaceutical industry, and the genome-editing, cell therapy, and immuno-oncology industries specifically, is characterized by intense competition and rapid innovation. Our potential competitors include major multi-national pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, and universities and other research institutions. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development staffs, established manufacturing capabilities and facilities, and experienced marketing organizations with well-established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies that have greater resources. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated on our competitors. Competition may increase further as a result of advances in the commercial applicability of genome editing or other new technologies and greater availability of capital for investment in these industries. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient enrollment for participation in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our development programs. In addition, due to the intense research and development taking place in the genome-editing field, including by us and our competitors, the intellectual property landscape is in flux and highly competitive. There may be significant intellectual property-related litigation and proceedings relating to our owned and in-licensed, and other third-party, intellectual property rights in the future. Our commercial opportunities could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, have broader acceptance and higher rates of reimbursement by third-party payors, or are less expensive than any product candidates that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, genome-editing technologies developed by our competitors may render our product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitor products. The key competitive factors affecting the success of our product candidates are likely to be their efficacy, safety, and availability of reimbursement.

Our focus is on the development of cell therapies using our chRDNA genome-editing technology. We are aware of several companies focused on developing therapies for various indications using CRISPR-Cas9 genome-editing technology including CRISPR Therapeutics AG, Editas Medicine, Inc., and Intellia. In addition, several academic groups have developed new genome-editing technologies based on CRISPR-Cas9, such as base editing and prime editing, as well as alternative CRISPR systems, which may have utility in therapeutic development. We believe companies such as Beam Therapeutics Inc., Metagenomi Technologies, LLC, Prime Medicine, Inc., and Scribe Therapeutics, Inc. are developing alternative CRISPR systems. Multiple academic labs and companies have also published on other CRISPR-associated nuclease variants that can edit human DNA. There are also companies developing therapies using non-CRISPR genome-editing technologies, such as transcription activator-like effector nucleases,

meganucleases, and zinc finger nucleases. These companies include bluebird bio, Inc., Allogene Therapeutics, Inc., Cellectis S.A., Precision BioSciences, Inc., and Sangamo Therapeutics. In addition to competition from other genome-edited therapies or gene or cell therapies, any product we may develop may also face competition from other types of therapies, such as small molecule, antibody, or protein therapies.

Our allogeneic CAR-T and CAR-NK cell therapy product candidates face significant competition from multiple companies, including Allogene, Atara Biotherapeutics, Inc., Cellectis, Celyad Oncology SA, CRISPR Therapeutics AG, Fate Therapeutics, Inc., Poseida Therapeutics, Inc., Precision BioSciences, and Sangamo Therapeutics. There are over 200 preclinical- and clinical-stage autologous and allogeneic anti-CD19 CAR-T programs, some of which will be competitive with our CB-010 product candidate, and over 90 preclinical- and clinical-stage autologous and allogeneic anti-BCMA CAR-T programs, some of which will be competitive with our CB-011 product candidate. Additionally, other companies are developing allogeneic CAR-T cell therapies for AML.

To become and remain profitable, we must develop and eventually commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. These activities may include completing preclinical studies and clinical trials of our product candidates; obtaining marketing and reimbursement approval for these product candidates; manufacturing, marketing, and selling those products that are approved; and satisfying any post-marketing requirements. We may never succeed in any or all these activities and, even if we do, we may never generate revenues that are significant enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the price of our common stock and could impair our ability to raise capital, maintain our research and development efforts, expand our business, or continue our operations. A decline in the price of our common stock also could cause stockholders to lose all or part of their investments.

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

Our business operations and current and future arrangements with clinical site investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we market, sell, and distribute our product candidates, if approved. Such laws include, but are not limited to, the U.S. Anti-Kickback Statute, U.S. civil and criminal false claims laws, the U.S. federal Beneficiary Inducement Statute, HIPAA, and state and local laws and regulations. Some of these laws may apply differently to, and may have different requirements for, and effects on, our business, rendering compliance complex and possibly burdensome. We cannot predict how future changes to these laws may impact our business.

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

Our business activities will be subject to U.S. export control licensing requirements, as well as other U.S. and foreign trade regulations, sanctions laws, anti-corruption laws, and anti-money laundering laws and regulations including the Foreign Corrupt Practices Act.

We develop product candidates that may be subject to U.S. export control licensing requirements and foreign investment regulations. Export licensing policies vary, and we may be unable to collaborate with certain countries or, if our product candidates receive regulatory approval, make sales to certain customers as a result of applicable license requirements. We also may incur increased compliance program costs in connection with U.S. export controls, and the availability of future investments from certain countries may be limited as a result of the controlled nature of our product candidates.

If we expand our business internationally or collaborate globally, we will be required to make investments in compliance programs related to U.S. international trade laws, including the FCPA and similar anti-bribery or anti-corruption laws, regulations, and rules of other countries in which we may choose to operate. Anti-corruption laws are interpreted broadly.

Our business is heavily regulated and therefore involves significant interaction with public officials, including, potentially in the future, officials of non-United States governments. Additionally, in many other countries, the healthcare providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, if our product candidates receive regulatory approval, our dealings with these prescribers and purchasers will be subject to regulation under the FCPA. We may engage third parties to sell our product candidates outside the United States if we receive regulatory approval in such jurisdictions for our product candidates. We may also have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. The SEC and the DOJ have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. For these reasons, we may be required to expend resources related to training and compliance under FCPA and other anti-corruption laws. There is no certainty that all our employees, suppliers, CMOs, CROs, or other third parties providing services to us will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of these activities.

If we have international activities in the future, we may be required to invest in compliance programs and resources related to U.S. import and export regulations, anti-money laundering laws, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls.

Violations of these international trade laws and regulations could result in fines; criminal sanctions against us, our management, or other employees; the closing down of facilities, including those of our suppliers and CMOs; requirements to obtain export licenses; cessation of business activities in sanctioned countries; implementation of compliance programs; and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to seek regulatory approval for our product candidates and, if such approval is received, to sell our products in one or more jurisdictions. This could materially damage our reputation, our ability to attract and retain employees, and our business, financial condition, results of operations, and prospects.

We face potential liability related to the privacy of health information we may obtain from the patients in our clinical trials.

Most healthcare providers are subject to privacy and security regulations promulgated under HIPAA, as amended by HITECH. We are not currently classified as a covered entity or business associate under HIPAA and thus are not subject to its requirements or penalties. However, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information. In addition, if we receive sensitive personally identifiable information, including health information, we may be subject to state laws requiring notification of affected individuals and state regulators if a breach of personal information occurs, which is a broader class of information than the health information protected by HIPAA.

We cannot assure you that we, our CROs, our clinical trial sites, and our clinical trial principal investigators with access to personally identifiable and other sensitive or confidential information relating to the patients in our clinical trials will not breach contractual obligations, or that we or they will not experience data security breaches or attempts thereof. This could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations as discussed above, which could in turn adversely affect our business, financial condition, results of operations, and prospects. We cannot assure you that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, storage, and transmission of such information.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which could have a material adverse effect on our business, financial condition, results of operations, or prospects.

The regulatory framework for the collection, use, safeguarding, sharing, transfer, and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, many jurisdictions have established their own data security and privacy frameworks. In the United States, there are a broad variety of data protection laws that are either currently in place or under way and a wide range of enforcement agencies at both the state and federal levels have the authority to review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission ("FTC"), and state Attorneys General have been aggressive in reviewing privacy and data security protections for

consumers. New laws also are being considered at both the state and federal levels. For example, the CCPA, which went into effect on January 1, 2020, provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. There also is the threat of consumer class actions related to these laws and the overall protection of personal data.

The data privacy laws in the EU have also been significantly reformed. The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the GDPR. 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 has expanded the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial patients and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the European Economic Area should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information or impose substantial fines for violations of the GDPR, which can be up to 4% of global revenues or €20 million, whichever is greater, and it 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. In addition, the GDPR provides that EU member states may make their own additional laws and regulations limiting the processing of personal data, including genetic, biometric, or health data.

Risks Relating to Our Intellectual Property

If we do not possess the necessary intellectual property rights covering our proprietary CRISPR chRDNA genome-editing technology and our product candidates, we may not be able to block competitors or to compete effectively in our markets.

Our industry is subject to rapid technological change and our success depends in large part on our ability to obtain and maintain intellectual property protection in the United States and other jurisdictions with respect to our CRISPR chRDNA platform technology and product candidates. We rely upon a combination of patents, owned by us or in-licensed from third parties, and trade secrets to protect our technology and product candidates. We seek to protect our proprietary position by filing patent applications in the United States and in other jurisdictions related to our genome-editing technologies and product candidates that are important to our business. We also rely on know-how and continuing technological innovation to develop and maintain our competitive position. If we are unable to obtain or maintain intellectual property protection with respect to our CRISPR chRDNA genome-editing platform technology and product candidates, our business, financial condition, results of operations, and prospects will be materially harmed.

The strength of patents in the biotechnology and pharmaceutical fields generally, and the genome-editing field in particular, involves complex legal and scientific questions and can be uncertain. For example, the scope of patent protection that will be available to us in the United States is uncertain. Changes in either the patent laws or their interpretation may diminish our ability to protect our intellectual property; obtain, maintain, defend, and enforce our intellectual property rights; and, more generally, could affect the value of our intellectual property or narrow the scope of our owned or in-licensed patents. With respect to both owned and in-licensed intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents, whether the claims of any issued patents will provide sufficient protection, or whether, if these patents are challenged by our competitors, they will be found to be invalid, unenforceable, or not infringed.

The patent prosecution process is expensive, time-consuming, and complex, and we or our licensors may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patents at a reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development in time to obtain patent protection before public disclosures are made. Although we may enter into non-disclosure or confidentiality agreements with parties who may have access to patentable aspects of our research and development, such as our employees, collaborators, CMOs, consultants, CROs, clinical trial site investigators and personnel, and other third parties, any one of these parties may breach their confidentiality agreements and disclose innovations before we can file a patent application, thereby jeopardizing our ability to seek patent protection.

The USPTO requires compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. The ultimate outcome of our pending patent applications is uncertain and the coverage claimed in a patent application can be significantly reduced before the patent is issued. Even as our patent applications, or those of our licensors, currently or in the future, issue as patents, they may not issue in a form that will provide us with any meaningful protection,

prevent competitors or other third parties from competing with us, dissuade companies from collaborating with us, or otherwise provide us with any competitive advantage. Periodic maintenance fees on issued patents are also required to be paid over the lifetime of the patent. Although an inadvertent lapse can, in many cases, be cured by payment of a late fee or by other means in accordance with applicable laws and regulations, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in the loss of patent rights. 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, nonpayment of fees, failure to properly legalize and submit formal documents, and the like. If we experience noncompliance events that cannot be corrected and we lose our patent rights, competitors could enter the market, which would have a material adverse effect on our business.

Composition of matter patents for biological and pharmaceutical products, such as CAR-based cell therapy products, often provide a strong form of intellectual property protection as such patents provide protection without specifying any particular method of use or manufacture. Methods of use patents can protect particular applications of a product or the manufacturing of a product; however, such method claims do not prevent a competitor from using a product that is identical to our product for an indication that is outside the scope of the patented method of use or making a product that is identical to our product using a different method of manufacturing. Our allogeneic CAR-T and CAR-NK cell therapy product candidates do not contain our chRDNA genome-editing technology; rather, our chRDNA guides are used in the manufacturing of our CAR-T and CAR-NK products. It is virtually impossible to determine whether a competitor has infringed our chRDNA patents in making their products. Thus, even if we obtain patent protection on certain aspects of our technologies, such protection may not be enough to block our competitors from entering the market.

Third-party claims of intellectual property infringement may prevent or delay our ability to commercialize our product candidates.

The fields of genome editing and CAR-T and CAR-NK cell therapies are relatively new. No genome-edited products have been commercialized and there is ongoing patent litigation in the autologous CAR-T cell therapy space. Due to the widespread research and development that is taking place in these fields, including by us and our competitors, the intellectual property landscape is in flux and may remain uncertain for the foreseeable future. There may be significant litigation and administrative proceedings that could affect our genome-editing technologies and product candidates.

Our commercial success depends upon our ability to develop, manufacture, market, and sell product candidates that we may develop or license and to use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our product candidates. As industry, government, academia, and other biotechnology and pharmaceutical research expands and more patents are issued, the risk increases that our genome-editing technologies or product candidates may give rise to claims of infringement of the patent rights of others. We cannot guarantee that our genome-editing technologies, current and future product candidates, or the use or manufacture of such product candidates does not currently or will not in the future infringe third-party patents. There may be third-party patents with claims to compositions, methods of manufacture, or methods of use or treatment that could cover our current or future product candidates. It is possible that we may fail to identify relevant third-party patents or applications. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Thus, we cannot be certain that we were the first to file any patent application related to our genome-editing technologies or product candidates. Furthermore, patent rights are granted jurisdiction-by-jurisdiction, and our freedom to practice certain genome-editing technologies, including our ability to research, develop, and commercialize our product candidates, may differ by country.

Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields of CRISPR genome editing as well as the field of immuno-oncology, including those relating to CAR constructs and CAR-T and CAR-NK cell therapy compositions and methods of use. Our CB-010 product candidate, which is an allogeneic anti-CD19 CAR-T cell therapy for the treatment of r/r B-NHL, uses Cas9 chRDNAs to insert the CD19-specific CAR into the T cell genome and for an additional edit. Numerous parties have intellectual property relating to RNA-guided Cas9 genome editing. See *Risk Factors - "Our ability to continue to receive licensing revenue and to enter into new licensing arrangements related to the foundational CRISPR-Cas9 intellectual property will be substantially impaired if such intellectual property is limited by administrative patent proceedings."* Our CB-011 product candidate and our CB-012 product candidate both use Cas12a chRDNAs to insert the CAR into the T cell genome and to make additional edits. We are aware of certain third-party patents assigned to the Broad Institute, Massachusetts Institute of Technology, and the President and Fellows of Harvard University relating to CRISPR-Cas12a genome-editing systems (Cas12a was then referred to as Cpf1), which will expire in late 2035 assuming no PTE or PTA. Additionally, we are aware of third-party patents assigned to the U.S. government relating to anti-BCMA CARs as well as nucleic acids encoding such CARs, vectors comprising these nucleic acids, and host cells expressing such CARs, which will expire in 2033 assuming no PTE or PTA. We are also aware of several third-party patents relating to various CAR compositions, methods of use, and components, including specific co-stimulatory regions. There is ongoing patent litigation over various third-party CAR patents, and unexpired patents that survive that litigation could be asserted against us.

Third parties may assert that our product candidates infringe their patents, including those listed above. Under U.S. patent laws, conducting clinical trials and seeking regulatory approval in the United States for therapeutic products are generally not considered an act of infringement, and similar exemptions are present in other countries. Nevertheless, third parties may allege that the act of filing our BLA or conducting clinical trials is outside of the safe harbor provision for activities reasonably related to the development and submission of information to the FDA for regulatory approval, and third parties may, upon our regulatory filing, assert infringement claims based on existing patents or patents that may be issued prior to our BLA filing, regardless of the merit of such claims. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, ownership, or priority. Patents 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. In order to successfully challenge the validity of any U.S. patent in federal court, we would need to overcome this presumption of validity, and there can be no assurance that a court of competent jurisdiction would invalidate the patent. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize any product candidates we may develop, including CB-010, CB-011, CB-012, and CB-020, as well as any other product candidates or technologies covered by the asserted third-party patents.

If any third-party patents were held by a court of competent jurisdiction to cover our genome-editing technology used in the manufacturing of our product candidates or any product candidate itself or its indication, the holders of those patents may be able to block our ability to commercialize the product candidate unless and until we obtained a license under the applicable patents, or the patents expire, or are held to be not infringed, unpatentable, invalid, or unenforceable. We may not be able to obtain a license to the blocking patents, or the terms of the license may not be commercially viable. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same intellectual property licensed to us, and it could require us to make substantial upfront, milestone, and royalty payments. 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 blocked or delayed, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We could also be forced, including by court order, to cease manufacturing and commercializing any infringing product candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed the third-party patent. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of our management time and resources from our business.

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

Filing, prosecuting, maintaining, enforcing, and defending patents on our genome-editing technologies and product candidates in countries outside the United States is expensive. Prosecution of patent applications is often a longer process and patents may grant at a later date, and with a shorter term, than in the United States. The requirements for patentability differ in certain jurisdictions and countries. Additionally, the patent laws of some countries do not afford intellectual property protection to the same extent as the laws of the United States. For example, unlike patent law in the United States, patent law in most European countries and many other jurisdictions precludes the patentability of methods of treatment and diagnosis of the human body. Other countries may impose substantial restrictions on the scope of claims, limiting patent protection to specifically disclosed embodiments. Consequently, we may not be able to prevent third parties from practicing our inventions in major markets outside the United States, or from selling or importing products 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 may export otherwise infringing products to jurisdictions 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 such competition. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in intellectual property laws in various jurisdictions worldwide.

Many companies have encountered significant problems in enforcing and defending intellectual property rights in various jurisdictions globally. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property rights generally. Proceedings to enforce our intellectual property rights in various jurisdictions globally 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, could put related 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 file, 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 against competitors.

Many jurisdictions have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties if they are not practicing the patented technology. In addition, some countries limit the enforceability of patents against third parties, including government agencies. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and

prospects may be adversely affected. Patent protection must be maintained on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain jurisdictions or countries, and we will not have the benefit of patent protection in such jurisdictions or countries.

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

We may in the future be subject to claims that former employees, consultants, or other third parties have an interest in our patents or other intellectual property as an inventor, co-inventor, or owner of trade secrets. Although it is our policy to require our employees and consultants who may be involved in the conception or development of intellectual property to execute agreements assigning that intellectual property to us, we may be unsuccessful in executing such an agreement with each party who conceives or develops intellectual property that we regard as our own or such party may breach the assignment agreement. We may have disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to obtain ownership or to defend against claims challenging inventorship. If we or our licensors fail in that litigation, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property or other proprietary information. Such an outcome could have a material adverse effect on our business. Even if we or our licensors are successful in defending against those claims, litigation could result in substantial costs and be a distraction to our management and other employees, and the claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

Although various extensions may be available, the term of a patent, and the protection it affords, is limited. In most countries including the United States, the natural expiration of a patent is generally 20 years after its first effective filing date. Our chRDNA genome-editing patents will expire in 2036, without any PTE. Even if patents covering our product candidates are obtained, once the patent term has expired for a product we may be open to competition from biosimilar or generic medications. In addition, although, upon issuance in the United States the term of a patent can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by us during patent prosecution or if terminal disclaimers are filed over other co-owned patents or patent applications to avoid rejections based on obviousness-type double patenting. If we do not have sufficient patent term to protect our products, our business, financial condition, results of operations, and prospects will be adversely affected.

We may not obtain patent term extension for any product candidates we develop.

Depending upon the timing, duration, and specifics of any FDA marketing approval of any product candidates we develop, our U.S. patents may be eligible for limited PTE under 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 clinical trials and the FDA regulatory review process. A PTE 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 a patent with claims covering the approved biologic, a method for its approved indication, 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 clinical 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 the applicable requirements. Moreover, we may not receive PTE or we may receive less time than we requested. If we are unable to obtain PTE or if the term of any such PTE is less than we request, we will be unable to rely on our patent position to forestall the marketing of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

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

Patent reform legislation in the United States and other countries could increase the uncertainties around patent protection, costs, and the enforcement or defense of our patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. For example, the 2011 Leahy-Smith America Invents Act included a number of significant changes to U.S. patent law. Such provisions affect the way patent applications are prosecuted, redefine prior art, and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith America Invents Act transformed the U.S. patent system from a first-to-invent to a first-to-file system, effective on March 16, 2013. For small companies, such as ours, this means that we must file our patent applications earlier in our development process rather than relying on proving priority of invention and it is now easier and less costly for third parties to attack our patents, all of which could harm our business, financial condition, results of operations, and prospects.

There is uncertainty regarding the patentability of certain inventions in the biotechnology and pharmaceutical areas. Recent decisions by the U.S. Supreme Court have either narrowed the scope of patent protection available in certain circumstances or weakened the rights of patent owners in particular situations. For example, in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the Supreme Court ruled that a "naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated," and invalidated Myriad Genetics' claims on isolated BRCA1 and BRCA2 genes. To the extent that our claims relate to naturally occurring antibodies or proteins, these may be deemed to be directed to natural products or to lack an inventive concept above and beyond an isolated natural product, and a court may decide the claims are invalid under Myriad. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO, and the relevant law-making bodies, as well as courts and patent offices in other countries, the laws and regulations governing patents could change in unpredictable ways that may weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future, which could have a material adverse effect on our existing patent portfolio and those of our licensors. Europe's Unified Patent Court may present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. Although this new court is being implemented to provide more certainty and efficiency to patent enforcement throughout Europe, it will also provide our competitors with a new forum to use to centrally challenge our patents, rather than having to seek invalidity or non-infringement decisions on a country-by-country basis. Once the Unified Patent Court is established, it will be several years before the scope of patent rights that will be recognized and the strength of patent remedies that will be provided is known.

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

Competitors may infringe our patents or our licensors' patents or challenge the validity of our or our licensors' patent rights. Even if our patents are unchallenged, they may not adequately prevent others from designing their products to avoid being covered by our claims. If the breadth or strength of protection provided by our patents and patent applications to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our or their ability to commercialize, our product candidates.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and likely to divert significant resources from our core business, including distracting our management and scientific personnel from their normal responsibilities, and generally harm our business. Additionally, a defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Thus, suing a third party for patent infringement puts our patents at risk and we may choose not to take such actions, thus allowing a competitor to infringe our patents. Grounds for a validity challenge in a counterclaim could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Thus, 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 one or more of our pending patent applications at risk of not issuing, all of which could negatively impact our business. Even if we establish infringement in a legal proceeding against a third party, the court may decide not to grant an injunction against further infringing activity by the defendant and may only award money damages, which may or may not be an adequate remedy for us depending on the circumstances. Furthermore, because of the substantial amount of discovery required in connection with U.S. patent litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation.

Third parties may also raise similar claims of invalidity before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include *inter partes* review, *ex parte* reexamination, and post grant review in the United States, and equivalent proceedings in foreign jurisdictions, including opposition proceedings before the EPO. These proceedings could result in revocation or amendment to our patents, which potentially could result in our patents no longer protecting our genome-editing technologies or our product candidates. A loss of patent protection could have a material adverse impact on our business.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. There can be no assurance that we will have sufficient financial or other resources for such litigation or proceedings, which may continue for several years. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing or misappropriating or successfully challenging our intellectual property rights. In addition, if securities analysts or investors perceive litigation results to be negative, it could have a substantial adverse effect on the price of our common stock. There could be public announcements of the results of litigation or patent challenge hearings, motions, or other interim proceedings or developments, which also could affect the price of our stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. Any of the foregoing could allow third parties to develop and commercialize competing technologies and products and have a material adverse impact on our business, financial condition, results of operations, and prospects.

Our product candidates are biologics, and as such, we may enter into a settlement agreement with a biosimilar manufacturer seeking to market a product highly similar to our product; such a settlement agreement may be reviewed by the Federal Trade Commission and such review could result in a fine or penalty and substantial expense.

The FTC reviews patent settlement agreements between biologics companies and biosimilar manufacturers to evaluate whether these agreements include, among other things, anti-competitive reverse payments that slow or defeat the introduction of lower-priced medicines, including biosimilars. If we are faced with an FTC challenge of a settlement agreement with a biosimilar manufacturer, such challenge could impact how or whether we settle the case and, even if we strongly disagree with the FTC's position, we could face a penalty or fine and substantial expense. Any litigation settlements we enter into with biosimilar manufacturers could also be challenged by third parties adversely affected by the settlement. These kinds of follow-on lawsuits, which may be class action suits, can be expensive and can continue over multiple years. If we were to face lawsuits of this nature, we may not be successful in defeating these claims and we may, therefore, be subject to large payment obligations, which we may not be able to satisfy in whole or in part.

Our rights to develop and commercialize our product candidates are subject to the terms and conditions of our licenses and assignments with third parties. If we fail to comply with our obligations under these agreements, we could lose intellectual property rights and be subject to litigation from our licensors or assignors.

We license, or have taken assignment to, patents related to certain of our product candidates and genome-editing technologies from third parties. These licenses and assignments typically impose obligations on us, including diligence and payment obligations. If we fail to comply with our obligations under these agreements, our licensors and assignors may have the right to terminate our agreements, in which case we would not be able to commercialize any product that is covered by the patent rights at issue. Additionally, we may be subject to litigation for breach of these agreements. Moreover, if disputes over intellectual property that we have licensed, or taken assignment of, prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the product candidates or technologies covered by such patents, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects. In addition, intellectual property rights that we license in the future may include sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. Should our licensors or any of the upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should those agreements be terminated or amended, our ability to develop and commercialize our product candidates may be materially harmed.

Our CRISPR chRDNA genome-editing patent family was developed under a three-year research collaboration between us and Pioneer, now Corteva Agriscience. Initially, this patent family was owned by Pioneer under the terms of the Pioneer Agreement with Pioneer (then a DuPont company), and Pioneer granted us an exclusive license to the chRDNA patent family in the fields of human and animal therapeutics and research tools as well as a non-exclusive license in certain other fields outside the Pioneer Exclusive Field. Through an amendment to the Pioneer Agreement, dated December 18, 2020, Pioneer assigned the chRDNA patent family to us in exchange for an upfront payment and potential future milestones. As part of this amendment, Pioneer also granted a covenant not to sue for our licensees of our chRDNA technology under certain other Pioneer intellectual property (to which we already have a license that, in this situation, we cannot sublicense to licensees of our chRDNA technology in the field of human therapeutics) that might cover our chRDNA genome-editing technology, provided that we make the required payments. Thus, if we do not make such payments, our licensees could be sued by Pioneer, which could result in our licensees suing us for breach of contract.

Additionally, under the Pioneer Agreement, we licensed certain Pioneer background CRISPR-Cas9 intellectual property, particularly a patent family owned by Vilnius University and exclusively licensed to Pioneer, that we have sublicensed to several third parties as part of our CRISPR-Cas9 out-licensing program. Although the Vilnius patent family does not cover our chRDNA genome-editing technology or product candidates, if we were to materially breach the Pioneer Agreement and not cure the breach, Pioneer could terminate the Pioneer Agreement, which would expose us to possible lawsuits from a number of our sublicensees to the Vilnius University patent family.

For our CB-011 product candidate, an allogeneic anti-BCMA CAR-T cell therapy, we took assignment of an anti-BCMA scFv from ProMab under the ProMab Agreement. Although we own the patent family that covers this scFv and its methods of use, if we materially breach, and do not cure, the ProMab Agreement, ProMab could terminate the agreement and we would be required to immediately cease any and all manufacture, sale, offer for sale, use, import, or export of products comprising the anti-BCMA scFv (provided that, if our product is approved for commercial sale, we may sell any remaining existing inventory of such products for a short period of time). If this were to happen prior to regulatory approval, we would not be able to continue the development of CB-011, and if this were to happen after regulatory approval, we would lose all future revenues from CB-011.

The scFv in our CB-012 product candidate, an allogeneic anti-CD371 CAR-T cell therapy, is exclusively licensed to us in this field by MSKCC. To maintain the license, we are required to pay annual license fees and to meet certain diligence milestones within specified periods of time. We may extend these periods by a certain number of months upon payment of additional fees. If we materially breach, and do not cure, the MSKCC Agreement, MSKCC may terminate the MSKCC Agreement, in which case we would not be able to continue the development of CB-012.

Thus, we are reliant upon the above licenses to and assignments of certain intellectual property from third parties that is important or necessary to the development of our genome-editing technologies and product candidates. In spite of our best efforts, our licensors or assignors might conclude that we have materially breached our license or assignment agreements, respectively, and might terminate these agreements, thereby removing our ability to develop and commercialize products and technology covered by the agreements. To the extent such third parties fail to meet their obligations under these agreements, which we are not in control of, we may lose the benefits of the agreements. If these agreements are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors could have the freedom to seek regulatory approval of, and to market, products identical to ours. Any of these events could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

Disputes may arise with the third parties from whom we license or take assignment of our intellectual property rights from for a variety of reasons, including:

- the scope of rights granted under the license or assignment agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on, or derive from, intellectual property of the licensor that is not subject to the license or assignment agreement and is not covered by a covenant not to sue;
- the sublicensing of rights and the obligations to our licensors associated with sublicensing;
- our diligence obligations under license or assignment agreements and what activities satisfy those diligence obligations; and
- whether payments are due and when.

We may not be successful in obtaining or maintaining necessary rights to any future product candidates that we acquire through acquisitions or in-licenses.

Our future programs may involve additional product candidates that may require the use of intellectual rights held by third parties, and the growth of our business could depend, at least in part, on our ability to acquire or in-license these proprietary rights. We may be unable to acquire or in-license intellectual property rights from third parties that we identify. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, which would harm our business. 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 case, we may be required to expend significant time and resources to develop or license other product candidates. We may need to cease development of a future product candidate covered by such third-party intellectual property rights.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies that 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 develop 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. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates or new genome-editing or other technologies that we may seek to acquire. If we are unable to successfully obtain rights to required third party intellectual property rights, we may not be able to expand our product pipeline, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our ability to continue to receive licensing revenue and to enter into new licensing arrangements related to the foundational CRISPR-Cas9 intellectual property will be substantially impaired if such intellectual property is limited by administrative patent proceedings.

We have an exclusive license from UC and Vienna in all fields to the CVC IP, having as inventors Drs. Jennifer A. Doudna, Emmanuelle Charpentier, Martin Jinek, and Krzysztof Chylinski. We have entered into over 20 sublicenses, both exclusive and non-exclusive, to this CRISPR-Cas9 intellectual property in combination with licenses to our own Cas9 intellectual property (and sometimes in combination with a sublicense to the Vilnius Cas9 patent family we licensed from Pioneer) in a variety of fields (e.g., human cell therapy, microbial applications, agriculture, livestock, industrial biotechnology, nutrition and health, research reagents and services, forestry, transgenic animal models, internal research, etc.). We are also required to share with UC/Vienna a percentage of sublicensing revenue we receive including cash and equity. These sublicense agreements are an important source of revenues for us while we are developing our own product candidates. Furthermore, we must reimburse UC/Vienna for the patent prosecution and maintenance costs associated with the CVC IP, which are substantial in light of all the disputes outlined below.

The CVC IP that we have exclusively licensed from UC/Vienna is co-owned with Dr. Charpentier, and Dr. Charpentier has not granted us any rights to the CVC IP, either directly or indirectly. On December 15, 2016, we entered into an IMA with UC, Vienna, Dr. Charpentier, CRISPR Therapeutics AG (the exclusive licensee of Dr. Charpentier in the field of human therapeutics), ERS Genomics Ltd (the exclusive licensee of Dr. Charpentier in all fields outside human therapeutics), and Intellia, our exclusive licensee in a defined field of human therapeutics. Under the IMA, the co-owners provided reciprocal worldwide cross-consents to each of the other co-owners' existing licensees and sublicensees as well as future licensees and sublicensees, with no accounting to the other owners. The IMA includes a number of other commitments and obligations with respect to supporting and managing the CVC IP, including a cost-sharing agreement. In the United States, each co-owner has the freedom to license and exploit the technology. As a result, although our license from UC/Vienna is exclusive, we do not have any rights from Dr. Charpentier and thus our license to the CVC IP from UC/Vienna is non-exclusive with respect to such co-owned rights. Furthermore, in the United States, each co-owner is required to be joined as a party to any claim or action we may wish to bring to enforce those patent rights. Although we have entered into the IMA, which provides for, among other things, notice of and coordination in the event of third-party infringement of the patent rights within the CVC IP, there can be no assurance that all parties will cooperate in any future infringement. In addition, the parties to the IMA may dispute certain provisions and the resolution of any contract interpretation disagreement could increase what we believe to be our financial obligations to UC/Vienna.

The CVC IP is, and has been, the source of several disputes in the USPTO, the EPO, and other patent offices. At the time the CVC IP was first filed (May 25, 2012), the United States was under a first-to-invent patent system; thus, if two or more patent applications or one or more patents and one or more patent applications claimed the same invention, the USPTO would determine the inventorship. Specifically, the Broad Institute Inc. and Massachusetts Institute of Technology and, in some instances, the President and Fellows of Harvard College (individually and collectively, the "Broad"), owns a patent family (having an earliest filing date of December 12, 2012) that includes issued patents in the United States and Europe that claim certain aspects of CRISPR-Cas9 systems to edit DNA in eukaryotic (i.e., plant and animal) cells, including human cells. In January 2016, the Patent Trial and Appeal Board ("PTAB") of the USPTO declared an interference (Interference No. 106,048, or the '048 interference) between one of the then-pending U.S. patent applications (now U.S. Patent No. 10,266,850) included in the CVC IP and 12 issued U.S. patents owned jointly by the Broad to determine which set of inventors invented first and, thus, was entitled to patents on the invention in the United States. The PTAB concluded at the end of the motions phase that the declared interference should be discontinued (and not progress to the priority phase) because the involved claim sets were considered patentably distinct from each other. Following appeal by the CVC group, in September 2018, the U.S. Court of Appeals for the Federal Circuit, affirmed the PTAB's decision to terminate the interference proceeding without determining which inventors actually invented the use of the CRISPR-Cas9 genome-editing technology in eukaryotic cells. In June 2019, the PTAB declared another interference (Interference No. 106,115, or the '115 interference) between 14 pending U.S. patent applications in the CVC IP and 13 patents and a patent application co-owned by the Broad. The Broad patents include those that were the subject of the '048 interference. In February 2022, the PTAB issued its decision that the Broad inventors were the first to invent the use of CRISPR-Cas9 genome editing in eukaryotic cells; the owners of the CVC IP plan to appeal this decision to the U.S. Court of Appeals for the Federal Circuit.

In addition to the Broad, ToolGen, Inc., MilliporeSigma (a subsidiary of Merck KGaA), and Harvard University, each filed patent applications claiming CRISPR-Cas9-related inventions after the CVC IP was first filed (October 23, 2012 in the case of ToolGen patent family; December 6, 2012 in the case of the MilliporeSigma patent family; and December 17, 2012 in the case of the Harvard University patent family) and have alleged that they invented one or more of the inventions claimed in the CVC IP before the CVC inventors did. In December 2020, the PTAB declared an interference (Interference No. 106,127, or the '127 interference) between a ToolGen patent application that claims certain aspects of CRISPR-Cas9 systems to edit DNA in eukaryotic cells, including human cells, and the same 14 pending U.S. patent applications in the CVC IP that are involved in the '115 interference. The motions phase of this interference has concluded, the parties have requested a hearing on the motions, and a decision will issue thereafter. Additionally, the PTAB declared an interference (Interference No. 106,126) at the same time between the same ToolGen patent application and the Broad patents and patent application in the '115 interference. In June 2021, the PTAB declared an interference

(Interference No. 106,132 or the ‘132 interference) between a MilliporeSigma patent application that claims methods for using CRISPR-Cas9 systems to edit DNA in eukaryotic cells, including human cells, and the same 14 pending U.S. applications in the CVC IP that are involved in the ‘115 and ‘127 interferences. This interference is currently in the motions phase. Also in June 2021, the PTAB declared an interference (Interference No. 106,133) between the same MilliporeSigma patent application and the Broad patents and patent applications in the ‘115 and ‘126 interferences. We do not know the impact, if any, that the recent PTAB decision in the ‘115 interference will have on the ‘127 interference or the ‘132 interference.

Opposition proceedings in the EPO have been initiated against patents owned by the Broad, ToolGen, and MilliporeSigma, and various third parties have opposed the three issued CVC European patents. Opposition proceedings can lead to the revocation of a patent in its entirety, the maintenance of the patent as issued, or the maintenance of a patent in amended form, and opposition proceedings and appeals therefrom typically take years to resolve. These CRISPR-Cas9 patents will expire in 2033 without PTA or PTE.

In light of the uncertainty surrounding the CVC IP, certain third parties have negotiated royalty-stacking provisions in their sublicenses with us, whereby they can deduct from what they owe to us a certain percentage of royalties they pay to other parties with CRISPR-Cas9 patents (such as to the Broad). Furthermore, other third parties have adopted a “wait and see” approach and are not entering into license agreements with us or third parties until all of the uncertainty surrounding inventorship and priority among the groups with CRISPR-Cas9 patents is resolved. If patents in the CVC IP are invalidated, certain of our sublicensees may wish to renegotiate their license agreements with us or may terminate for convenience. If this happens prior to commercialization of our own product candidates, we could lose a source of revenues while still remaining responsible for reimbursing UC for costs of prosecuting and maintaining the remaining CVC IP.

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

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets and confidentiality 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. Trade secrets and know-how can be difficult to protect.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure or confidentiality agreements with parties who have access to them, such as our employees, collaborators, CMOs, CROs, clinical trial site personnel and investigators, consultants, and other third parties. We also enter into confidentiality and invention assignment agreements with our employees and our agreements with consultants include invention assignment obligations. We seek to preserve the integrity and confidentiality of our data, know-how, and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in these individuals, organizations, and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breaches. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets.

Despite these efforts, any of these parties may breach agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for any breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts both within and outside the United States may be less willing or unwilling to protect proprietary information and trade secrets. If a competitor lawfully obtains or independently develops any of our trade secrets, we will have no right to prevent that competitor from using such information to compete with us, which could harm our competitive position. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we may not be able to establish or maintain a competitive advantage in our markets, which could materially adversely affect our business, operating results, financial condition, and prospects. Additionally, it is possible that our genome-editing technology platform, our trade secrets, and our know-how will over time be disseminated within the industry through the publication of journal articles and the movement of personnel from our company into academia or into other companies that may be our competitors.

Furthermore, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA’s disclosure policies may change in the future, if at all. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position will be materially and adversely harmed.

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

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

- others may be able to make, use, and sell cell therapy products that are similar to our product candidates without infringing our intellectual property rights;
- others may independently develop similar or alternative genome-editing technologies without infringing our intellectual property rights;
- we may not develop additional proprietary technologies that are patentable;
- others may misappropriate our trade secrets, or independently develop or acquire our trade secrets lawfully; and
- our patents may have expired, whether or not PTE was granted.

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

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

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

Risks Relating to Our Relationships with Third Parties

We rely on third parties to supply the materials for, and the manufacturing of, our clinical product candidates, and, if such product candidates receive regulatory approval, we may continue our reliance on third parties for manufacturing of our commercial products.

We currently do not have clinical-scale manufacturing capabilities, nor do we have any immediate plans to develop such capabilities; thus, we must rely on third-party CMO to manufacture clinical supplies for our product candidates. We currently rely on five different CMOs to supply materials to an additional CMO who manufactures the necessary CB-010 cell therapy product candidate materials for our ANTLER phase 1 clinical trial. We anticipate that we may need to engage other suppliers and CMOs, for our clinical trials with our CB-011 and CB-012 product candidates.

We receive the CRISPR chRDNA guides used for genome editing from one CMO, the Cas protein (Cas9 in the case of CB-010) from another CMO, the virus used to insert the CAR into the T cell genome from another CMO located outside the United States, and our healthy donor cells from two different sources owned by the same third-party supplier. The virus CMO receives plasmid from another supplier used in the manufacture of the viral material. Another CMO uses all of these materials to manufacture the CAR-T products for our ANTLER clinical trial for our CB-010 product candidate. Coordination is essential to ensure that the various materials are received by the CMO manufacturing the T cell products in time, and in the correct amounts, for manufacturing runs. The manufactured CAR-T products then undergo a series of release testing. There can be no assurance that we will not experience supply or manufacturing issues in the future; particularly, given our reliance on single-source suppliers, some of which are small companies with limited resources and experience to support clinical, and ultimately commercial, products. We cannot ensure 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 purposes. In addition, the lead time needed to establish a relationship with a new supplier can be lengthy, and we may experience delays in meeting demand if we must switch to a new supplier or CMO. The time

and effort to qualify a new supplier or CMO, including to meet any regulatory requirements for such qualification, could result in additional costs, diversion of resources, or reduced manufacturing yields, any of which would negatively impact our operating results. Furthermore, we may be unable to enter into agreements with a new supplier on commercially reasonable terms, which could have a material adverse impact on our business, financial condition, results of operations, and prospects.

If our CMOs and suppliers cannot successfully manufacture materials that conform to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure or maintain regulatory approval for their manufacturing facilities. In addition, we have no direct control over the ability of our CMOs and suppliers to maintain adequate quality control, quality assurance, and corresponding maintenance of records and documents, or to hire and retain trained personnel. If the FDA or a foreign regulatory authority inspects these third-party facilities for compliance with regulations for the manufacture and testing of materials or product candidates and, if these facilities fail inspection and cannot adequately correct deficiencies, we may need to find alternative CMOs, which would significantly impact our ability to develop and obtain regulatory approval for our product candidates, and if approved, to market our products. In addition, if our CMOs and suppliers are unable to timely perform or have operations temporarily halted as a result of inspection or enforcement actions taken by the FDA or other regulatory authorities, or as a result of the COVID-19 pandemic, we may experience manufacturing delays or delays in receiving healthy donor cells used in manufacturing our CB-010 product candidate or may need to find alternative CMOs or suppliers, which in each case would significantly impact our ability to develop, obtain regulatory approval for, and market our product candidates, if approved.

We do not yet have sufficient information to reliably estimate the cost of the commercial manufacturing of our product candidates, and the actual cost to manufacture and process our product candidates could materially and adversely affect the commercial viability of our product candidates. Our product candidates have not been manufactured at commercial scale, may not be able to achieve commercial manufacturing, and we may be unable to create a product inventory necessary to satisfy demands for any of our product candidates following approval. As a result, we may never be able to develop a commercially viable product.

In addition, our current reliance on a limited number of CMOs and suppliers exposes us to a variety of risks, each of which could delay our preclinical studies, clinical trials, the approval, if any, of our product candidates by the FDA or foreign regulatory authorities, or the commercialization of our product candidates or result in higher costs or deprive us of potential product revenue. These risks include:

- our CMOs and suppliers may be unable to timely manufacture our product candidates or produce the quantity and quality required to meet our preclinical, clinical, and commercial needs, if any;
- our CMOs and suppliers may not be able to execute our manufacturing procedures appropriately;
- our CMOs and suppliers have their own proprietary methods, which we may not have access to if we wish to, or are required to, switch CMOs or suppliers. Additionally, we may not own, or may have to share, the intellectual property rights to any improvements made by our CMOs in the manufacturing process for our product candidates;
- our CMOs and suppliers may not perform as agreed or may not remain in business for the time required to supply our clinical trials or to successfully manufacture, store, and distribute our commercial products;
- our CMOs and suppliers could breach or terminate their agreements with us;
- we face competition for supplies from other gene and cell therapy companies, which may make it difficult for us to secure materials or the testing of such materials on commercially reasonable terms or in a timely manner;
- our CMOs may fail to adequately store the various components received from our suppliers and any damage or loss of such materials could materially impact our ability to manufacture and supply our product candidates;
- we rely on third parties to perform release tests on our product candidates prior to delivery to clinical trial sites. If these tests are not appropriately done and test data are not reliable, patients could be put at risk of serious harm;
- we may be unable to identify additional CMOs or suppliers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA or foreign regulatory authorities may have questions regarding any replacement CMO or supplier. This may require new testing and regulatory interactions. In addition, a new CMO would have to be educated in, or develop substantially equivalent processes for, production of our product candidates; and
- as a result of the current COVID-19 pandemic, our CMOs and suppliers may experience production delays and shutdowns.

Our CMO that supplies the virus we use to insert the CAR into our CB-010 CAR-T product candidate is located outside the United States. To date, our virus CMO has not been audited by the FDA, but it has received the cGMP certification for the manufacture of recombinant viral vectors from an EU national regulatory authority. There are additional risks with using a non-U.S. vendor, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs, and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- trade protection measures, import, or export licensing requirements, or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- difficulties in managing international logistics and transportation; and
- workforce uncertainty in countries where labor unrest is more common than in the United States.

For our allogeneic CAR-T product candidates, we rely on receiving healthy donor material to manufacture our product candidates. Variation in quality of donor T cells, and potential challenges in procuring appropriate donor material, could result in insufficient product supply or may result in us being unable to initiate or continue clinical trials on the timelines we expect.

Unlike autologous CAR-T companies, we are reliant on receiving healthy donor material to manufacture our product candidates. Healthy donor T cells vary in quality, and this variation requires us to release batches with the highest integrity based on specifications confirmed by regulatory authorities, which makes producing standardized product candidates more likely. However, this step may slow the development and commercialization pathway of those product candidates if releasable batches are not identified sufficiently rapidly. We and our CMOs have developed a screening process designed to enhance the quality and consistency of T cells used in the manufacture of our CAR-T cell product candidates, but our screening process may fail to identify suitable donor material and we may discover failures with the material after production. We may also have to develop new testing methods and update our specifications for new risks, such as screening for new viruses. We have strict specifications for donor material, which include specifications required by regulatory authorities. If we are unable to (i) identify and obtain donor material that satisfies specifications, (ii) agree with regulatory authorities on appropriate specifications, or (iii) address variability of donor T cells, there may be insufficient material or we may be unable to initiate or continue clinical trials on the timelines we expect, which could harm our reputation and adversely impact our business and prospects. Although our suppliers are currently able to provide us with donor material, if, in the future, our suppliers are unable to secure donor material due to the COVID-19 pandemic or for other reasons, we may no longer have sufficient donor material to manufacture our cell therapy product candidates.

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

We depend, and will continue to depend, on CROs, clinical trial sites and clinical trial principal investigators, contract laboratories, and other third parties to conduct our ANTLER phase 1 clinical trial for our CB-010 product candidate and future clinical trials for our other product candidates. We will rely heavily on these third parties over the course of our clinical trials, and we control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the protocol and applicable legal, regulatory, and scientific standards and regulations, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with cGCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for the conduct of clinical trials on product candidates in clinical development. Regulatory authorities enforce cGCPs through periodic inspections and for-cause inspections of clinical trial principal investigators and trial sites. If we or any of these third parties fail to comply with applicable cGCPs or fail to enroll a sufficient number of patients, we may be required to conduct additional clinical trials to support our marketing applications, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal, state, or foreign fraud and abuse or false claims laws and regulations or healthcare privacy and security laws, or provide us or government agencies with inaccurate, misleading, or incomplete data.

Although we intend to design the clinical trials for our product candidates, our CROs will facilitate and monitor our clinical trials. As a result, many important aspects of our clinical development programs, including site and investigator selection, and the conduct and timing and monitoring of the study, will be partly or completely outside our direct control. Our reliance on third parties to conduct clinical trials will also result in less direct control over the collection, management, and quality of data developed through clinical trials than would be the case if we were relying entirely upon our own employees. Communicating with third parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities.

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 these third parties, we cannot control whether they devote sufficient time and resources to our ongoing preclinical, clinical, and nonclinical programs. 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 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 if there are other difficulties with such third parties, such as staffing difficulties, changes in priorities, or financial distress, our clinical trials may be extended, delayed, or terminated. As a result, 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 will be harmed, our costs could increase, and our ability to generate revenue could be delayed.

If any of our relationships with trial sites, or any CRO that we may use in the future, terminates, we may not be able to timely enter into arrangements with alternative trial sites or CROs, or do so on commercially reasonable terms. Switching or adding clinical trial sites or CROs to conduct our clinical trials involves substantial cost and requires extensive management time, training, and focus. In addition, there is a natural transition lag when a new third party must learn about our product candidates and protocols, which can result in delays that may materially impact our ability to meet our desired clinical development timelines.

We also are required to register certain ongoing clinical trials and post the results of completed clinical trials on a U.S. government-sponsored database, www.ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions. Our ANTLER phase 1 clinical trial for our CB-010 product candidate is posted on www.ClinicalTrials.gov. For any violations of laws and regulations during the conduct of our preclinical studies and clinical trials, we could be subject to warning letters or enforcement action that may include civil and other penalties, up to and including criminal prosecution.

We may not be able to meet our obligations under the AbbVie collaboration or our own product candidates and pipeline may be delayed in light of our obligations to AbbVie. In addition, we have limited control over the achievement of milestones by AbbVie.

In February 2021, we entered into a multi-year collaboration and license agreement under which we will utilize our CRISPR Cas12a chRDNA genome-editing and cell therapy technologies to research and develop two new CAR-T cell therapies for AbbVie. We are responsible for conducting certain preclinical research, development, and manufacturing activities, including assisting in the manufacturing of all phase 1 clinical materials and assisting AbbVie with the preparation and filing of its IND applications. We and AbbVie have developed a detailed research plan and budget for the first of the two program slots; provided, however, that AbbVie may choose to delay certain research activities, which will affect the amount of reimbursement we receive from AbbVie as well as the timing of future milestone payments. The collaboration involves a substantial number of our employees and resources, although we are reimbursed by AbbVie for our work on the collaboration. We have not previously undertaken a collaboration of this magnitude and focus. Although we continue to hire employees to increase our research and development group, it is not certain that we will be able to timely hire, or retain, qualified employees, in which case the work on our pipeline products may be delayed until we are able to increase our staff such that we can meet our obligations under the AbbVie research plan and continue to develop our own product candidates. In addition, our ability to receive significant milestone payments upon AbbVie's achievement of developmental, regulatory, and sales-based milestones is outside our control and is dependent on AbbVie's commercially reasonable efforts to develop, commercialize, and manufacture the licensed collaboration products.

We may form or seek collaborations or strategic alliances in the future for the development and commercialization of one or more of our product candidates or for new product candidates. We may not be successful in those efforts and, even if we do enter into any collaborations, they may not be successful.

Our product candidate development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. To date, we have not partnered with a third party with respect to any of our product candidates. In the future, we may choose to partner with third parties for one or more of our product candidates. If we are unable to negotiate and enter into partnerships, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential

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

If we decide to collaborate with pharmaceutical or biotechnology companies for the development and potential commercialization of any of our product candidates, or new product candidates, we may not be able to negotiate collaborations for such product candidates on a timely basis, on acceptable terms, or at all. We may also be restricted under existing agreements from entering into future collaborations. Collaborations are complex and time-consuming to negotiate and document. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the potential collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the potential collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by FDA or comparable regulatory authorities outside the United States, the potential market for the subject product candidate or candidates, the costs and complexities of manufacturing and delivering such product candidates to patients, the potential of competing biologics or other therapeutic approaches, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than one with us for our product candidate or for a new product candidate. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Thus, we may face significant competition in seeking appropriate collaborators.

Furthermore, the terms of any collaborations or other arrangements that we may establish may not be favorable to us. Even if we are able to enter into a collaboration, the following are some of the risks associated with doing so:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations and may not devote sufficient resources to the development, manufacturing, marketing, or sale of collaboration products;
- collaborators may not pursue development and commercialization of any product candidates we may develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require further development of a product candidate for clinical testing;
- collaborators may adopt alternative technologies, which could decrease the marketability of our product candidates and genome-editing technologies;
- collaborators may independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours, that may result in the withdrawal of the collaborator support for our collaboration product candidates;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of our product candidates;
- collaborators may not properly obtain, maintain, enforce, or defend our intellectual property if we grant such rights or may use our intellectual property in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or expose us to potential litigation;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change in control;
- disputes may arise between our collaborator and us that may cause the collaborator to act in a manner adverse to us and could result in the delay or termination of the research, development, or commercialization of our product candidates or that result in costly litigation or arbitration that diverts our management's attention and resources;

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

- collaboration agreements may be terminated and, if terminated, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, resulting in a need for additional capital to pursue further development or commercialization of the applicable product candidates we may develop.

We may not realize the benefits of acquired assets or other strategic transactions.

We evaluate various strategic transactions on an ongoing basis. We may acquire other businesses, products or product candidates, intellectual property, or technologies as well as pursue joint ventures or investments in complementary businesses. The success of any future strategic transaction depends on various risks and uncertainties, including:

- unanticipated liabilities related to acquired companies or joint ventures;

- difficulties integrating acquired personnel, technologies, and operations into our existing business;

- retention of key employees;

- diversion of management's time and focus from operating our business to management of strategic alliances or joint ventures or acquisition integration challenges;

- increases in our expenses and reductions in our cash available for operations and other uses;

- disruption in or termination of our relationships with collaborators or suppliers as a result of such a transaction; and

- possible write-offs or impairment charges relating to acquired businesses or joint ventures.

Foreign acquisitions and joint ventures are subject to additional risks, including those related to integration of operations across different cultures and languages, currency risks, potentially adverse tax consequences of overseas operations, and the particular economic, political, and regulatory risks associated with specific countries.

Future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of debt, contingent liabilities, or amortization expenses or write-offs of goodwill, any of which could harm our financial condition. We could also incur losses resulting from undiscovered liabilities that are not covered by the indemnification we may obtain from the seller.

If we in-license product candidates or products or acquire businesses, we may not be able to realize the benefit of those transactions if we are unable to successfully integrate them with our existing operations and company culture. We cannot be certain that, following a strategic transaction or license, we will achieve the results, revenue, or specific net income that justifies the transaction. Future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of debt, contingent liabilities, or amortization expenses or write-offs of goodwill, any of which could harm our financial condition.

We may be subject to claims that our employees, consultants, or third parties performing services for us have wrongfully used or disclosed confidential information of third parties.

Many of our employees were previously, and our consultants are or were previously, employed at universities or research institutions, or at other biotechnology or pharmaceutical companies. Although we try to ensure that our employees, consultants, and third parties performing services for us do not use the proprietary information or know-how of former employers or other companies in their work for us, we may be subject to claims that we or these individuals have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer or other third party. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our management and employees.

Risks Relating to Employee Matters, Managing Growth, and Other Risks Relating to Our Business

Our future success depends on our ability to retain our executive officers and to attract, retain, and motivate qualified personnel.

We are highly dependent on the research and development, clinical, operational, legal, financial, and other business expertise of our executive officers, including Rachel E. Haurwitz, Ph.D., our president and chief executive officer; Steven B. Kanner, Ph.D., our chief scientific officer; Ruhi Khan, M.B.A., our chief business officer; Barbara G. McClung, J.D., our chief legal officer and corporate secretary; Jason V. O'Byrne, M.B.A., our chief financial officer; and Syed Rizvi, M.D., our chief medical officer, as well as other members of our senior leadership team and our scientists. Certain of our scientists have greatly contributed to our intellectual property and are critical as we move our CRISPR Cas12a chRDNA technology platform forward. Although we have entered into employment agreements with all of our executive officers, each of them may terminate their employment with us at any time. All of our employees are "at will," which means that any of our employees could leave our employment at any time, with or without notice.

We conduct substantially all of our operations at our facilities in Berkeley, California. The San Francisco Bay Area is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel in our industry is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms, if at all. Many of the biotechnology companies and research institutions that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. Recruiting and retaining qualified research, development, manufacturing, regulatory, and clinical personnel is critical to our success. Our success also depends on our ability to continue to attract, retain, and motivate entry-level, mid-level, and senior scientific personnel as well as managers. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies, as well as academic and research institutions, for similar personnel. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can discover and develop product candidates and operate our business will be limited.

To induce employees to remain at our company, in addition to salary and cash incentives, we provide equity awards that vest over time, the value of which may be significantly affected by movements in our stock price that are beyond our control and may be insufficient to counteract more lucrative offers from other companies.

In addition, we rely on consultants and advisors, including our co-founders and scientific advisory board, or SAB, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, including Drs. Jennifer A. Doudna and Martin Jinek, who are among our founders and who are pioneers in CRISPR genome-editing technology, are not employed by us, are employed by employers other than us, and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

The inability to recruit or retain certain executive officers, key employees, consultants, or advisors may impede the progress of our research, development, and commercialization objectives and have a material adverse effect on our business, intellectual property, financial condition, results of operations, and prospects.

We must continue developing and expanding our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

As of February 1, 2022, we had 99 full-time employees, and we expect to continue to increase our number of employees and the scope of our operations in 2022 and beyond as we seek to advance development, and if successful, commercialization, of our product candidates. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational, and financial systems; expand our facilities; and continue to recruit and train additional qualified personnel. Current and future growth imposes significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining, motivating, and integrating additional employees;
- managing our internal development efforts effectively, including clinical trials and FDA or foreign regulatory authority review for our product candidates, while complying with our contractual obligations to third parties; and
- improving our operational, financial and management controls, reporting systems, and procedures.

Also, our management may need to divert a disproportionate amount of its attention away from their day-to-day activities and devote a substantial amount of time to managing these expansion activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among our remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial

resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage this expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the continuing development and expansion of our company.

Our internal computer systems, or those of our third-party vendors, collaborators, consultants, or third parties performing services for us, may fail or suffer security breaches, which could result in a material disruption of the development of our product candidates and program research, compromise sensitive information related to our business, or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.

Our internal computer systems and those of our current and any future third-party vendors, collaborators, consultants, and third parties performing services for us, as well as our clinical sites and regulatory authorities, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, and telecommunication and electrical failures. In addition, the COVID-19 pandemic has intensified our dependence on information technology systems as many of our critical business activities are currently being conducted remotely.

Although we have not experienced any such material system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our product candidate development and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from our current or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in the theft or destruction of intellectual property, data, or other misappropriation of assets; financial loss; or otherwise compromise our confidential or proprietary information and disrupt our operations, our competitive position could be harmed, and the further development and commercialization of our product candidates could be delayed.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification, or intentional or accidental release or loss of information maintained in the information systems and networks of our company, our third-party vendors, and clinical sites, including personal information of our employees and, potentially, our clinical study patients, and company and vendor confidential data. In addition, third parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our personnel or the personnel of our vendors to disclose sensitive information to gain access to data and systems. We may experience threats to our data and systems, including malicious codes and viruses, phishing, and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our information technology systems or those of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks.

In addition, we could be subject to regulatory actions or claims made by individuals and groups in private litigation involving privacy issues related to data collection and use practices and other data privacy laws and regulations, including claims for misuse or inappropriate disclosure of data, as well as unfair or deceptive practices. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls, and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated.

Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. As we outsource more of our information systems to vendors, engage in more electronic transactions with clinical sites and collaborators, and rely more on cloud-based information systems, the related security risks will increase and we will need to expend additional resources to protect our technology and information systems. In addition, there can be no assurance that our internal information technology systems, or those of third parties with which we conduct business, will be sufficient to protect us against breakdowns, service disruption, data deterioration, or loss in the event of a system malfunction, or prevent data from being stolen or corrupted in the event of a cyberattack, security breach, industrial espionage attacks, or insider threat attacks, which could result in financial, legal, business, or reputational harm.

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

We are exposed to the risk of fraud or other misconduct by our employees, clinical trial principal investigators, and consultants. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in other jurisdictions, to provide accurate information to the FDA and other regulatory authorities, to comply with healthcare fraud and abuse laws and regulations in the United States and in other jurisdictions, to report financial information or data accurately, or to disclose unauthorized activities to us. Such misconduct could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We may also be subject to federal, state, and foreign laws governing the privacy and security of identifiable patient information. If our operations are found to be in violation of any of these laws that apply to us, we may be subject to significant administrative, civil, and criminal penalties. If we commercialize our products, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements.

We have adopted a Code of Business Conduct, Scientific and Data Integrity, and Ethics that is applicable to all of our employees, but it is not always possible to identify and deter employee misconduct. The precautions we take to detect and prevent misconduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations, and prospects, including the imposition of administrative, civil, and criminal penalties; damages; monetary fines; contractual damages; reputational harm; and curtailment of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

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 harm our business; additionally, our business could be shut down until we are in compliance with those laws and regulations.

We are subject to numerous federal, state, and local 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 materials. Our operations also produce hazardous waste products. We contract with third parties for the disposal of these materials and wastes. We will not be able to eliminate the risk of contamination or injury from these materials. If contamination or injury results from any use by us of hazardous materials, we could be held liable for any resulting damages. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with these laws and regulations. In addition, we may incur substantial costs to comply with current or future environmental, health, and safety laws and regulations. These current or future laws and regulations may impair our product candidate development and research program efforts.

Moreover, there is increasing stakeholder pressure on companies to diligence environmental, social, and governance matters in the supply chain. Negative publicity regarding production methods, alleged practices, or workplace or related conditions of any of our suppliers, CMOs, CROs, or third parties who perform services for us could adversely affect our reputation. We could be forced to locate alternatives, which could increase our costs and result in delayed supply of components for, and manufacturing of, our product candidates, or other disruptions to our operations.

Our insurance policies are expensive and only protect us from some business risks, which may leave us exposed to certain uninsured liabilities.

Although we have obtained product liability insurance coverage for our clinical trials, it may not be adequate to cover all expenses or liabilities that we may incur. Furthermore, we anticipate that we will need to increase our insurance coverage if we successfully commercialize any product candidate. Product insurance coverage is increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Once, and if, we obtain marketing approval for a product candidate, we intend to acquire product liability insurance coverage for our commercial products; however, we may be unable to obtain such product liability insurance on commercially reasonable terms or in adequate amounts. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. Additionally, we may have to pay amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Many of our license agreements require us to indemnify our licensors or licensees against certain third-party claims; we may not have insurance for those indemnifications or our insurance may be inadequate should any claim arise.

As a public company, it is expensive for us to maintain and, in the future, increase our levels of director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same

or similar coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash position and results of operations. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees, or as executive officers.

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

We will face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if such product candidates receive marketing approval and are sold commercially. 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 claims that our product candidates caused injuries, we could incur substantial liabilities. Even a successful defense would require significant financial and management resources. Regardless of merit or eventual outcome, liability claims may result in:

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

As a public company, we are obligated to develop and maintain proper and effective internal controls over financial reporting, and any failure to maintain the adequacy of these internal controls may adversely affect investor confidence in our company and, as a result, the value of our common stock.

We will be required, pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), to furnish a report by management on, among other things, the effectiveness of our internal controls over financial reporting as of December 31, 2022, which is the year covered by the second annual report following the completion of our initial public offering. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal controls over financial reporting. In addition, our independent registered public accounting firm will be required to attest to the effectiveness of our internal controls over financial reporting in our first annual report required to be filed with the SEC following the date we are no longer an emerging growth company if we are not a non-accelerated filer at such time.

If we or our independent registered public accounting firm determines we have a material weakness in our internal controls over financial reporting, investors could lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the SEC or other regulatory authorities. Failure to remedy any material weakness or significant deficiency in our internal controls over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of amounts accrued on our financial statements.

In addition to federal income tax, we are subject to taxation in various state and local tax jurisdictions. As a result, our effective tax rate is derived from a combination of applicable tax rates in the locations in which we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each jurisdiction using rates based on prior experience. Nevertheless, our effective tax rate may be different than what we have experienced in the past due to numerous factors, including the passage of new tax legislation, changes in the mix of our profitability, if any, from jurisdiction to jurisdiction, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods and may result in tax obligations in excess of amounts accrued in our financial statements.

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

We have generated, and expect to continue to generate in the future, significant federal and state net operating loss ("NOL") carryforwards that are available to offset taxable income in future years, if any. We have also generated, and expect to continue to generate in the future, significant federal and state research and development tax credit carryforwards that are available to potentially offset federal income taxes and state income taxes, respectively, in future years, if any.

Under the Tax Cuts and Jobs Act of 2017 ("TCJA"), as modified by the Coronavirus Aid, Relief and Economic Security Act (the "CARES Act"), our federal NOLs incurred in taxable years beginning after December 31, 2017 may be carried forward indefinitely. Additionally, for tax years beginning after December 31, 2020, the deductibility of federal NOLs incurred in taxable years beginning after December 31, 2017 is limited to 80% of our taxable income. Also, NOLs that we incurred in 2018, 2019, and 2020 may be carried back five taxable years. It is uncertain if and to what extent various states will conform to the NOL changes contained in the TCJA and the CARES Act. Federal research and development credit carryforwards may only be carried forward for 20 years and therefore could expire unused. As a result, they may be unavailable to offset future taxes.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Tax Code"), and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percentage point change, by value, in its equity ownership by certain stockholders over a rolling three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. We have experienced prior ownership changes in 2014 and 2016. A Section 382 analysis was performed for the period January 1, 2021 through December 31, 2021, which concluded that we had experienced an additional "ownership change" upon our IPO in July 2021. We do not expect our tax attributes to expire unused. We have recorded a full valuation allowance for deferred tax assets, including NOLs and tax credits as of December 31, 2021. The issuance of common stock in the future, or shifts in the ownership of our common stock among certain stockholders, either separately or in combination, over time may result in a limitation under Sections 382 and 383 of the Code. In addition, at the state level, there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, California has imposed limits on the use of California state NOLs and tax credits to offset California taxable income in years beginning after 2019 and before 2023. If an ownership change occurs and we earn taxable income in future years, the limitation on our ability to use our NOLs and other tax attribute carryforwards could adversely affect our future operating results by increasing our future income tax liabilities. See Note 14 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information.

The COVID-19 pandemic or other pandemics or public health crises may adversely impact our business, financial condition, and results of operations, including our preclinical studies and clinical trials, and may cause substantial disruption in the financial markets and adversely impact economies worldwide.

We may experience disruptions related to the COVID-19 pandemic or other pandemics or public health crises that could severely impact our business, preclinical studies, clinical trials, and commercialization activities, including:

- halting or suspending enrollment in our clinical trials;
- delays or difficulties in enrolling and retaining patients in our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring and efficacy, safety and translational data collection, processing and analyses, due to limitations on travel imposed or recommended by federal, state, or local governments, employers and others or interruption of clinical trial subject visits, which may impact the collection and integrity of subject data and clinical study endpoints;
- requirements to change the ways in which our preclinical studies and clinical trials are conducted due to governmental regulations as part of a response to the COVID-19 pandemic or other pandemics or other public health crises, which may result in unexpected costs, delays, or discontinuation of our preclinical studies and clinical trials altogether;

- increased adverse events and deaths in our clinical trials due to COVID-19-related or other pandemic-related infections, which may result in increased complications due to immunosuppression from our lymphodepletion regimen;
- increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID-19 or being forced to quarantine due to other public health crises;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies and necessary interactions with such regulatory agencies due to limitations in employee resources, limitations on travel, forced furlough of government employees, or diversion of resources, which would impact review and approval timelines;
- interruption of, or delays in receiving, supplies of components for our product candidates from our suppliers, including the supply of healthy donor cells, and delays or suspension in manufacturing by our CMOs due to staffing shortages, production slowdowns or stoppages, and disruptions in delivery systems, or due to prioritization of production for COVID-19-specific (or other pandemic-related) therapies or vaccines;
- limitations on employee resources that would otherwise be focused on advancing our business, including because of sickness of employees or their families, including our executive officers and other key employees, the desire of employees to avoid contact with large groups of people, an increased reliance on working from home, or mass transit disruptions; and
- significant disruptions and volatility in the financial markets.

The COVID-19 pandemic continues to evolve. The extent to which the COVID-19 pandemic may impact our business, research, preclinical studies and clinical trials, productivity of our employees, supply chains, and access to capital or business development activities will depend on future developments, which are highly uncertain at this time. To the extent the COVID-19 pandemic adversely affects our business, financial condition, results of operations, and prospects, it may also have the effect of amplifying many of the other risks described in this *Risk Factors* section, such as those relating to the timing and results of our current and future clinical trials and our financing needs. See the *Impact of the COVID-19 Pandemic* in the *Management's Discussion and Analysis of Financial Condition and Results of Operations* section in Part II, Item 7 of this Annual Report on Form 10-K for more information about the impact of COVID-19 on our business.

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

In addition to the business disruptions caused by the COVID-19 pandemic or potential cybersecurity attacks, our operations, and those of our suppliers, CMOs, CROs, and clinical trial sites, could be subject to disruptions, including those caused by earthquakes, power shortages or outages, telecommunications failures, water shortages or outages, floods, hurricanes, typhoons, fires, extreme weather conditions, epidemics and pandemics, and other natural or man-made disasters or business interruptions. The occurrence of any of these business disruptions could seriously harm our business, financial condition, results of operations, and prospects, and increase our costs and expenses. Our ability to manufacture our product candidates could be disrupted if our operations or those of our suppliers, CMOs, CROs, or clinical trial sites are affected by a natural or man-made disaster or other business interruption. Our corporate headquarters are located in California near major earthquake faults and fire zones. The ultimate impact on us and our general infrastructure of being located near major earthquake faults and fire zones and being consolidated in certain geographical areas is unknown, but our business, financial condition, results of operations, and prospects could suffer in the event of a major earthquake, fire, or other natural disaster. Furthermore, our preclinical work involves studies in mice. In the past, vivarium sites have been shut down by animal activists, and any disturbance or shut down at sites where our preclinical work is being conducted could jeopardize our data and affect our product candidate timelines.

Furthermore, we interact with the FDA and other federal, state, and regulatory agencies, and lack of funding for such agencies or temporary shutdowns can affect our operations. 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, and has had to furlough critical government employees and stop critical activities. 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; statutory, regulatory, and policy changes; and business disruptions, such as those caused by the COVID-19 pandemic. Average review times at the agency have fluctuated in recent years as a result. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions for our product candidates, which could have a material adverse effect on our business.

Unfavorable global economic conditions could adversely affect our business, financial condition, or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn, inflation, or other global financial crises, could result in a variety of risks to our business, including weakened demand for our product candidates, if approved, or our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers and CMOs, possibly resulting in supply or manufacturing disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which such conditions could adversely impact our business.

Risks Relating to Ownership of our Common Stock

The market price of our common stock has been, and may continue to be, volatile and investors may suffer substantial losses if the price of our common stock drops significantly.

Some of the factors that may cause the market price of our common stock to fluctuate include:

- the timing and results of preclinical studies and clinical trials for any product candidates that we develop;
- delay, failure, or discontinuation of any of our product candidates or research programs;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- adverse regulatory decisions, including failure to receive regulatory approval of one or more of our product candidates;
- unanticipated or serious safety concerns related to our product candidates;
- developments or changing views regarding the use of biologics, including those that involve genome editing;
- commencement or termination of collaborations;
- regulatory or legal developments in the United States and other countries;
- assertions that our product candidates infringe third-party patents;
- invalidity challenges to our intellectual property, including intellectual property that we have in-licensed;
- manufacturing delays;
- acceptance or lack of acceptance of allogeneic products;
- inability to meet the obligations under our collaboration agreement with AbbVie;
- inability to obtain additional collaboration partners;
- the recruitment and retention of key personnel;
- the level of expenses related to any of our product candidates, including preclinical studies and clinical trials, as well as the level related to our research programs;
- the results of our efforts to develop additional product candidates or technologies;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcements or expectations of additional financing efforts;
- significant lawsuits, including contract disputes with our licensors, licensees, assignors, assignees, suppliers, CMOs, CROs, clinical sites, or stockholder litigation;
- sales of our common stock by us, our insiders, or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;

- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this *Risk Factors* section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations, including recently in connection with the COVID-19 pandemic. Broad market and industry factors, including potentially worsening economic conditions and other adverse effects or developments, may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert our management's attention and resources from our business.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

We currently have research coverage by a few industry and financial analysts. If any of those analysts discontinue coverage, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline.

If a significant amount of our shares of common stock are sold, or it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. As of March 17, 2022, we had 60,663,581 shares of common stock outstanding. Most of these shares can be sold at any time unless held by one of our affiliates, in which case the resale of those securities will be subject to volume limitations and other restrictions under Rule 144 of the Securities Act of 1933, as amended (the "Securities Act"). We have also registered all shares of common stock that we may issue under our equity compensation plans or that are issuable upon exercise of outstanding options or other equity awards. Therefore, these shares can be freely sold in the public market upon issuance and, once vested, subject to volume limitations applicable to our affiliates. If significant amounts of our shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

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

We are an "emerging growth company," as defined in the JOBS Act, and may remain an emerging growth company for up to five years following our IPO. For as long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act; not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements; reduced disclosure obligations regarding executive compensation; and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders will be different than the information that is available with respect to some other public companies. We have not included in this Annual Report on Form 10-K all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we 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.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to 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 we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our consolidated financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

We have incurred, and will continue to incur, increased costs as a result of operating as a public company, and our management will continue to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an "emerging growth company," we have and will continue to incur significant legal, accounting, and other expenses that we did not incur as a private company. The Dodd-Frank Wall Street Reform and Consumer Protection Act, the Sarbanes-Oxley Act, the listing requirements of Nasdaq, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We have had to hire additional accounting, finance, legal, and other personnel in connection with our efforts to comply with the requirements of being, a public company. Our management and other personnel devote a substantial amount of time toward maintaining compliance with these requirements. These requirements have increased our legal and financial compliance costs and have made some activities more time-consuming and costly. Operating as a public company also makes it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain coverage. This may make it more difficult for us to attract and retain qualified people to serve on our board of directors or as executive officers.

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

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

We do not expect to pay any dividends for the foreseeable future. Investors may never obtain a return on their investment.

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

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

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

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

- specify that special meetings of our stockholders can be called only by our board of directors, the chair of our board, or our chief executive officer;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder matters to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may be removed only for cause;
- expressly authorized our board of directors to make, alter, amend, or repeal our amended and restated bylaws; and
- require supermajority votes of the holders of our common stock to amend our amended and restated bylaws and specified provisions of our amended and restated certificate of incorporation.

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

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

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

As a California-domiciled public company, we were required to have at least two women and at least one director from an underrepresented community on our board of directors by the end of 2021; and we will have ongoing obligations to maintain a diverse board under California law and applicable Nasdaq rules.

Our success depends in part on our continued ability to attract, retain, and motivate highly qualified individuals to our board of directors. As a public company headquartered in California, we were required to have at least two women and at least one director from an underrepresented community on our board of directors by the end of 2021. Depending upon the size of our board of directors, we will be required to have two or three directors from underrepresented communities by the end of 2022. Although we currently have five women and two individuals from underrepresented communities on our board of directors, in the future we may be unable to recruit and retain diverse board members, and failure to comply with this California requirement could result in financial penalties. In addition, Nasdaq currently requires listed companies to disclose certain information about board of director diversity in company SEC reports.

Additionally, in August 2021, the SEC announced that it had approved Nasdaq's proposed rule change to advance board diversity and enhance transparency of board diversity statistics through new listing requirements. Under these new listing rules, we are now required to annually disclose diversity statistics regarding our directors' voluntary self-identified characteristics and to have at least one diverse director by the later of August 7, 2023, or the date on which we file our annual proxy statement in 2023 (or explain why we do not have one such director) and two diverse directors, including one who self-identifies as female and one who self-identifies as either an underrepresented minority or LGBTQ+, by August 6, 2025, or the date on which we file our annual proxy statement in 2025 (or explain why we do not have two such directors).

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, executive officers, or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative claim or action or proceeding brought on our behalf;
- any claim or action asserting a breach of fiduciary duty or aiding and abetting a breach of fiduciary duty;
- any claim or action against us arising under the Delaware General Corporation Law, our amended and restated certificate of incorporation, or our amended and restated bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

This provision would not apply to suits brought to enforce a duty or liability created by the Securities Act or the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation further provides that the federal district courts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. Although the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving the action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

This exclusive forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, executive officers, or other employees, which may discourage lawsuits against us and our directors, executive officers, and other employees. If a court were to find the exclusive forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

Item 1B. Unresolved Staff Comments.

Not applicable

Item 2. Properties.

Our corporate headquarters are located in Berkeley, California, where we lease approximately 61,735 square feet of research and development, laboratory, and office space pursuant to a lease agreement executed in March 2021 and expiring in March 2031. We have the ability to extend this lease for an additional five years until March 2036. See Note 9 to the consolidated financial statements included in this Annual Report on Form 10-K for additional information.

On January 13, 2022, we entered into a new lease agreement for 10,000 square feet of laboratory and office space near our current corporate headquarters. We will commence paying rent for this facility in August 2022. This lease expires in July 2032, and we have a one-time option to extend the term for an additional five years. See Note 17 to the consolidated financial statements included in this Annual Report on Form 10-K for additional information.

We believe that our existing facilities are adequate for our near-term needs and that suitable additional facilities will be available in the future if and when needed.

Item 3. Legal Proceedings.

From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Regardless of the outcome, litigation can have a material adverse effect on us due to defense and settlement costs, diversion of management resources, and other factors. We are not currently subject to any material legal proceedings.

Intellia Arbitration

In October 2018, Intellia initiated an arbitration proceeding (the "Intellia Arbitration") with JAMS asserting that we had violated the terms and conditions of the Intellia Agreement. The Intellia Arbitration focused on whether two patent families relating, respectively, to CRISPR-Cas9 chRDNA guides and Cas9 scaffolds, are included in the Intellia Agreement. In September 2019, we received an interim award from the arbitration panel determining that the two patent families are included in the Intellia Agreement, but the panel granted us an exclusive leaseback to Cas9 chRDNA guides under economic terms to be negotiated by the parties. In February 2020, the arbitration panel clarified that the leaseback relates solely to our CB-010 product candidate and instructed the parties to negotiate economic terms based on a leaseback of that scope. In June 2021, we entered into a Leaseback Agreement with Intellia, which granted us of an exclusive license to certain intellectual property relating to CRISPR-Cas9, including Cas9 chRDNAs, for use solely in the manufacture of our CB-010 product candidate in return for an upfront cash payment of $1.0 million and up to $23.0 million in potential future regulatory and sales milestones and low- to mid-single-digit percent royalty payments on net sales of our CB-010 product candidate by us, our affiliates, and sublicensees. The Leaseback Agreement resolved the dispute and, in July 2021, the arbitration panel dismissed the Intellia Arbitration with prejudice. See the *"Strategic Agreements - Intellia Therapeutics Inc. ("Intellia")"* section in Item 1 of this Annual Report on Form 10-K and Notes 4 and 9 of the consolidated financial statements included in this Annual Report on Form 10-K for additional information.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Our common stock is traded on the Nasdaq Global Select Market under the symbol "CRBU."

Holders

As of March 17, 2022, we had approximately 64 holders of record of our common stock. This number does not include beneficial owners whose shares were held in street name by banks, brokers, and other financial institutions.

Dividend Policy

We have not declared or paid cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends to holders of common stock in the foreseeable future.

Securities authorized for issuance under equity compensation plans

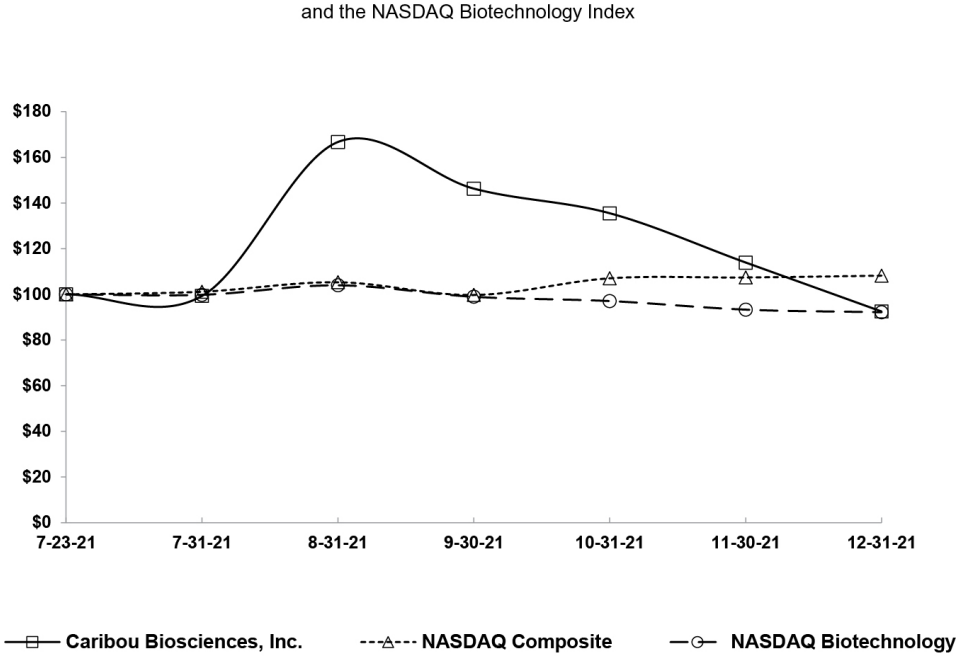
Information about securities authorized for issuance under our equity compensation plans is incorporated herein by reference to Part III, Item 12 of this Annual Report on Form 10-K.

Stock Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Exchange Act, nor shall such information be incorporated by reference into any future filing under the Exchange Act or the Securities Act, except to the extent that we specifically incorporate it by reference into such filing.

The graph set forth below compares the cumulative total stockholder return on our shares between July 23, 2021 (the first date for which a closing price is available on Nasdaq) and December 31, 2021, with the cumulative total return of (i) the Nasdaq Biotechnology Index and (ii) the Nasdaq Composite Index, over the same period. This graph assumes the investment of $100 on July 23, 2021 in our common stock and on June 30, 2021 in the Nasdaq Biotechnology Index and the Nasdaq Composite Index. It also assumes the reinvestment of dividends, if any. The graph assumes our closing sales price on July 23, 2021 of $16.32 per share as the initial value of our common stock and not the initial offering price to the public of $16.00 per share. The comparisons shown in the graph below are based upon historical data. The stock price performance included in this graph is not necessarily indicative of future stock price performance.

Comparison of Total Return Among Caribou Biosciences, Inc., the NASDAQ Composite Index, and the NASDAQ Biotechnology Index



	Cumulative Total Returns						
	7/23/21	7/31/21	8/31/21	9/30/21	10/31/21	11/30/21	12/31/21
Caribou Biosciences, Inc.	$ 100	$ 99	$ 167	$ 146	$ 135	$ 114	$ 92
NASDAQ Composite	$ 100	$ 101	$ 105	$ 100	$ 107	$ 107	$ 108
NASDAQ Biotechnology	$ 100	$ 100	$ 104	$ 99	$ 97	$ 93	$ 92

Use of Proceeds from our IPO

On July 22, 2021, our Registration Statement on Form S-1 (File No. 333-257604) relating to our IPO of our common stock was declared effective by the SEC. On July 22, 2021, we filed a second Registration Statement on Form S-1 (File No. 333-258105) pursuant to Rule 462(b) of the Securities Act, which was effective immediately upon filing. Our net proceeds from our IPO, after deducting underwriting discounts and commissions and estimated offering expenses of $28.6 million, were $321.0 million. We are holding a significant portion of the balance of the net proceeds from our IPO in money market funds and marketable securities. There has been no material change in our planned use of the net proceeds from our IPO from that described in the final prospectus for our IPO filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on July 23, 2021.

Recent Sales of Unregistered Securities

Set forth below is information regarding unregistered securities sold by us since January 1, 2021 (not previously reported on a quarterly report on Form 10-Q), for which common share numbers and stock option exercise prices have been adjusted, as appropriate, to reflect the 1.818-for-1 forward stock split which became effective on July 15, 2021:

1. In March 2021, we issued an aggregate of 6,663,940 shares of our Series C preferred stock to 36 accredited investors at a purchase price of $17.257 per share, for aggregate consideration of $115.0 million. In connection with the closing of our IPO, all 6,663,940 shares of Series C preferred stock automatically converted into 26,234,654 shares of our common stock.

2. During the three-month period ended March 31, 2021, we granted stock options to purchase an aggregate of 1,561,079 shares of our common stock at a weighted-average exercise price of $4.11 to employees and directors.

3. During the three-month period ended March 31, 2021, we issued an aggregate of 5,463,536 shares of our common stock to current and former employees, executive officers, and consultants upon their exercise of stock options, for aggregate cash consideration of approximately $9.3 million.

None of the foregoing transactions involved any underwriters or any public offering. These transactions were exempt from registration under the Securities Act in reliance on Section 4(a)(2) of the Securities Act (and Regulation D promulgated thereunder) or Rule 701 promulgated under Section 3(b) of the Securities Act as transactions by an issuer not involving any public offering or under benefit plans and contracts relating to compensation as provided under Rule 701.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. [Reserved]

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes included in this Annual Report on Form 10-K. This discussion and analysis contain forward-looking statements, including statements regarding our intentions, plans, objections and expectations for our business. Forward-looking statements are based upon current beliefs, plans and expectations related to future events and our future financial performance and are subject to risks, uncertainties and assumptions. Our actual results and the timing of certain events could differ materially from those described in or implied by these forward-looking statements as a result of various factors, including those set forth in the "Risk Factors" section of this Annual Report on Form 10-K. See also the Special Note Regarding Forward-Looking Statements section of this Annual Report on Form 10-K.

This section includes a discussion of 2021 and 2020 items and a comparison of the fiscal years ended 2021 and 2020. For a discussion of 2019 items and a comparison of the fiscal years ended 2020 and 2019, refer to the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of the final prospectus for our IPO filed with the SEC on July 23, 2021.

Overview

We are a clinical-stage genome-editing biopharmaceutical company dedicated to developing transformative CRISPR therapies for patients with devastating diseases. We are advancing a pipeline of allogeneic, or off-the-shelf, CAR-T and CAR-NK cell therapies for the treatment of patients with hematologic malignancies and solid tumors. Our renowned founders, including a Nobel laureate, are pioneers in the field of CRISPR genome editing. Our CRISPR chRDNA technology has demonstrated superior specificity and high efficiency in preclinical studies and enables us to perform multiple, precise genomic edits, while maintaining genomic integrity.

We believe that our technology has broad potential to generate gene and cell therapies in oncology and in therapeutic areas beyond oncology. Potential applications include immune cell therapies, cell therapies derived from genome-edited iPSCs, and *in vivo* genome-edited therapies.

We are initially focused on advancing multiple proprietary allogeneic cell therapies for the treatment of both hematologic malignancies and solid tumors against cell surface targets for which autologous CAR-T cell therapeutics have previously demonstrated clinical proof of concept, including both CD19 and BCMA, and other targets. We use our chRDNA technology to enhance, or armor, our cell therapies with multiple strategies, such as checkpoint disruption and immune cloaking, to improve persistence of antitumor activity.

Since our founding in 2011, we have devoted substantially all of our resources to organizing and staffing, business planning, raising capital, developing our genome-editing platform technologies, developing our product candidates and building our pipeline, creating and maintaining our intellectual property portfolio, and establishing arrangements with third parties for the manufacture and testing of our product candidates. We do not have any products approved for commercial sale and have not generated any revenue from product sales. We have incurred net losses since commencement of our operations.

To date, we have primarily funded our operations through revenue from our license agreements, license and collaboration agreements, and a service agreement; the sale of shares of Intellia common stock that we received as consideration for the Intellia License Agreement; the sale of our convertible preferred stock in private placements; and proceeds from our IPO. In total, we received an aggregate of approximately $321.0 million in net proceeds from our IPO, after deducting underwriting discounts and commissions and offering expenses. In connection with the closing of our IPO, all outstanding shares of our convertible preferred stock automatically converted into 26,234,654 shares of our common stock.

Our net losses for the years ended December 31, 2021 and 2020 were $66.9 million and $34.3 million, respectively. Our net losses and operating losses may fluctuate from quarter to quarter and year to year depending primarily on the timing of our clinical trials and nonclinical studies and our other research and development expenses. In addition, we are incurring increased costs associated with operating as a public company, including legal, audit, and accounting fees; regulatory costs related to maintaining compliance with the rules and regulations of the SEC and Nasdaq; director and officer insurance premiums; costs for investor and

public relations activities; and other accompanying compliance and governance costs. We anticipate that our expenses will increase substantially if and as we:

- progress our ANTLER phase 1 clinical trial for our CB-010 product candidate;
- continue our current research programs and our preclinical and clinical development of our other current product candidates, including CB-011, CB-012, and CB-020, and any other product candidates we identify and choose to develop;
- hire additional clinical, quality control, and scientific personnel;
- seek to identify additional research programs and additional product candidates;
- further develop our genome-editing technologies;
- acquire or in-license technologies;
- expand, maintain, enforce, and defend our intellectual property estate;
- seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical trials, if any;
- establish and expand manufacturing capabilities and supply chain capacity for our product candidates;
- add operational, legal, financial, and management information systems and personnel;
- experience any delays, challenges, or other issues associated with any of the above, including the failure of clinical trials meeting endpoints, the generation of unanticipated preclinical results or clinical trial data subject to differing interpretations, or the occurrence of potential safety issues or other development or regulatory challenges;
- make royalty, milestone, or other payments under current, and any future, in-license or assignment agreements;
- establish a sales, marketing, and distribution infrastructure to commercialize any product candidates for which we obtain marketing approval; and
- continue to operate as a public company.

We do not own or operate any manufacturing facilities and we outsource a substantial portion of our clinical trial studies to third parties. We use multiple CMOs to individually manufacture, under cGMP, chRDNA guides, Cas proteins, and AAV6 vectors used in the manufacture of our CAR-T cells as well as our CAR-NK cell therapy product candidates. We expect to rely on our CMOs for the manufacturing of our product candidates to expedite readiness for future clinical trials, and most of these CMOs have capabilities for commercial manufacturing. Additionally, we may decide to build our own manufacturing facility in the future to provide us greater flexibility and control over our clinical or commercial manufacturing needs.

Because of the numerous risks and uncertainties associated with therapeutic product development, we may never achieve profitability and, unless and until we are able to develop and commercialize our product candidates, we will need to continue to raise additional capital. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through public or private equity or debt financings, collaborations, strategic alliances, and licensing arrangements with third parties. There are no assurances that we will be successful in obtaining an adequate level of financing to support our business plans when needed on acceptable terms, or at all. If we raise additional funds through collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs, or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise capital as and when needed or on attractive terms, we may have to significantly delay, reduce, or discontinue the development and commercialization of our product candidates or scale back or terminate our pursuit of new in-licenses and acquisitions.

Impact of the COVID-19 Pandemic

The COVID-19 pandemic has caused governments worldwide to implement measures to slow the spread of the outbreak through travel restrictions, business shutdowns, and other measures. In response to the COVID-19 pandemic, starting on March 17, 2020, our entire workforce began working remotely pursuant to state, county, and city requirements. Since May 2020, we have gradually brought back on site all of our research employees whose work must be performed in the lab, and most of our non-research

employees are currently working partially remotely and partially on site. At this point in time, we do not know if or when we will bring our off-site functions back on site full-time. We have experienced no significant workforce reduction as a result of the COVID-19 pandemic.

The COVID-19 pandemic did have an impact on our supply chain in the early months of the pandemic. For example, we experienced delays in receiving healthy donor cells used in the manufacture of our CB-010 product candidate. These issues were largely resolved in 2021 and we are currently receiving adequate supplies of donor cells; however, we could face similar obstacles in the future. Although vaccines are now being distributed and administered across many parts of the world, new variants of the virus have emerged, and may continue to emerge, that are more contagious. As a result of future developments in the COVID-19 pandemic, we and our CMOs, CROs, clinical trial sites, and other third-party vendors may face disruptions that could delay or otherwise affect our ability to initiate and complete preclinical studies or clinical trials.

Since the start of the COVID-19 pandemic, we have been and will continue to be focused on the safety of our employees. In response to the COVID-19 pandemic, we have instituted on-site protocols and procedures in accordance with guidance provided by the Centers for Disease Control and the State of California and regulations and guidelines promulgated by the County of Alameda and the City of Berkeley. As of January 1, 2022, all of our employees were required to be fully vaccinated against COVID-19 as a condition of employment with us. Individuals who are unable to be vaccinated, due to a religious belief or disability that prevents them from being vaccinated, can request a reasonable accommodation.

In May 2020, we received a Paycheck Protection Plan ("PPP") loan from the Small Business Administration (the "SBA") in the amount of $1.6 million (the "PPP Loan"), which we used exclusively to pay employees' salaries. In December 2020, we submitted an application to have our PPP Loan forgiven and, on May 22, 2021, our PPP Loan was forgiven in full by the SBA.

To the extent the COVID-19 pandemic adversely affects our business prospects, financial condition, and results of operation, it may also have the effect of exacerbating many of the other risks described or referenced in the *Risk Factors* section in Item 1A of this Annual Report on Form 10-K, such as those relating to the timing and results of our planned and future clinical trials and our financing needs.

Components of Results of Operations

Licensing and Collaboration Revenue

We have not generated any revenue from product sales to date and do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval and commercialization, we may generate revenue in the future from product sales. We cannot predict if, when, or to what extent we will generate revenue from the commercialization and sale of our product candidates if we succeed in obtaining regulatory approval for these product candidates.

To date, all of our revenue consists of licensing and collaboration revenue earned from collaboration and/or licensing agreements entered into with third parties, including related parties. Under these agreements, we license rights to certain intellectual property controlled by us. The terms of these arrangements typically include payments to us of one or more of the following: nonrefundable, upfront license fees or exclusivity fees; annual maintenance fees; regulatory and/or commercial milestone payments; research and development payments; and royalties on the net sales of products and/or services. Each of these payments results in licensing and collaboration revenue. Revenue under such licensing and collaboration agreements was $9.6 million and $12.4 million for the years ended December 31, 2021 and 2020, respectively. See Note 4 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information.

For the foreseeable future we expect substantially all of our revenue will be generated from licensing and collaboration agreements.

Operating Expenses

Research and Development Expenses

Our research and development expenses consist of internal and external expenses incurred in connection with the development of our product candidates, development of our platform technologies, and our in-licensing and assignment agreements.

External costs include:

- costs associated with acquiring technology and intellectual property licenses that have no alternative future uses;
- costs incurred in connection with the preclinical and clinical development of our product candidates, including under agreements with CROs and other third parties that conduct clinical trials on our behalf;
- costs of supplying the components for, and the manufacturing of, our product candidates for use in our preclinical studies and clinical trials; and
- other research and development costs, including laboratory materials and supplies, and consulting services.

Internal costs include:

- employee-related costs, including salaries, benefits, and share-based compensation expense, for our research and development personnel; and
- allocated facilities and other overhead expenses, including expenses for rent and facilities maintenance and depreciation.

We expense research and development costs as incurred. Costs of certain activities are recognized based on an evaluation of the progress to completion of specific tasks. However, payments made prior to the receipt of goods or services that will be used or rendered for future research and development activities are deferred and capitalized as prepaid expenses and other current assets on our consolidated balance sheets. The capitalized amounts are recognized as expense as the goods are delivered or as related services are performed. Historically, we have not tracked external costs by clinical program. We intend to separately track certain external costs for each clinical program. However, we do not currently track, and do not intend to track, costs that are deployed across multiple programs.

Research and development activities are central to our business model. 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 for the foreseeable future as we continue to implement our business strategy; advance our CB-010 product candidate through clinical trials and later stages of development; conduct preclinical studies and clinical trials for our other product candidates; seek regulatory approvals for any product candidates that successfully complete clinical trials; expand our research and development efforts and incur expenses associated with hiring additional personnel to support our research and development efforts; and seek to identify, in-license, acquire, and/or develop additional product candidates.

The successful development of our CB-010, CB-011, CB-012, and CB-020 product candidates, as well as other potential future product candidates, is highly uncertain. Accordingly, at this time, we cannot reasonably estimate or know the nature, timing, and costs of the efforts that will be necessary to complete the development of our product candidates. We are also unable to predict when, if ever, we will generate revenue and material net cash inflows from the commercialization and sale of any of our product candidates for which we may obtain marketing approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs, and timing of preclinical studies, clinical trials, and development of our product candidates will depend on a variety of factors, including:

- sufficiency of our financial and other resources;
- acceptance of our CRISPR chRDNA genome-editing technology;
- ability to develop differentiating features so that our products have a competitive edge;
- completion of preclinical studies;
- establishment, maintenance, enforcement, and defense of our patents and other intellectual property rights;
- our ability to not infringe, misappropriate, or otherwise violate third-party intellectual property rights;
- clearance of IND applications to initiate clinical trials on product candidates;
- successful enrollment in, and completion of, our clinical trials on our product candidates;

- data from our clinical trials that support an acceptable risk-benefit profile of our product candidates for the intended patient populations and that demonstrate safety and efficacy;
- entry into collaborations to further the development of our product candidates or for the development of new product candidates;
- successful development of our internal process development and transfer to larger-scale facilities;
- establishment of agreements with CMOs for clinical and commercial supplies and scaling up manufacturing processes and capabilities to support our clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- grant of regulatory exclusivity for our product candidates;
- establishment of sales, marketing, and distribution capabilities necessary for commercialization of our product candidates if and when approved, whether by us or in collaboration with third parties;
- maintenance of a continued acceptable safety profile of our products post-approval;
- acceptance of our product candidates, if and when approved by the applicable regulatory authorities, by patients, the medical community, and third-party payors;
- ability of our products to compete with other therapies and treatment options;
- establishment and maintenance of healthcare coverage and adequate reimbursement; and
- expanded indications and patient populations for our products.

The following table summarizes our research and development expenses for the years ended December 31, 2021 and 2020:

	Years Ended December 31,		
	2021	2020	Change
		(in thousands)	
External costs:			
Expenses related to licenses, sublicensing revenue, and milestones	$ 3,960	$ 6,935	$ (2,975)
Services provided by CROs, CMOs, and other third parties that conduct preclinical studies and clinical trials on our behalf	20,032	9,900	10,132
Other research and development expenses	9,393	4,636	4,757
Total external costs	33,385	21,471	11,914
Internal costs:			
Personnel-related expenses	13,361	8,794	4,567
Facilities and other allocated expenses	5,509	4,160	1,349
Total internal costs	18,870	12,954	5,916
Total research and development expenses	$ 52,255	$ 34,425	$ 17,830

General and Administrative Expenses

Our general and administrative expenses consist primarily of personnel-related costs, intellectual property costs, consulting costs, and allocated overhead, including rent, equipment depreciation, and utilities. Personnel-related costs consist of salaries, benefits, and stock-based compensation for our general and administrative personnel. Intellectual property costs include expenses for filing, prosecuting, and maintaining patents and patent applications, including certain patents and patent applications that we license from third parties. We are entitled to receive reimbursement from third parties of a portion of the costs for filing, prosecuting, and maintaining certain patents and patent applications. We accrue for these reimbursements as the respective expenses are incurred and classify such reimbursements as a reduction of general and administrative expenses. During the years ended December 31, 2021 and 2020, we recorded $7.1 million and $5.8 million, respectively, of patent cost reimbursements as a reduction to general and administrative expense.

We expect that our general and administrative expenses will increase substantially in the future as a result of expanding our operations, including hiring personnel, preparing for potential commercialization of our product candidates, and additional facility occupancy costs, as well as increased costs associated with operating as a public company (including legal, audit, and accounting fees; regulatory costs related to maintaining compliance with the rules and regulations of the SEC and Nasdaq; director and officer insurance premiums; costs for investor and public relations activities; and other accompanying compliance and governance costs). We also expect to increase the size of our administrative function to support the growth of our business.

Other Income (Expense)

Other income (expense) consists primarily of interest income earned on cash and marketable securities, change in the fair value of our equity investments, change in fair value of the MSKCC success payments liability under the MSKCC Agreement, a gain on the PPP Loan extinguishment, and other income from the sale of certain intellectual property rights.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020:

	Years Ended December 31,		Change
	2021	2020	$
		(in thousands)	
Licensing and collaboration revenue	$ 9,598	$ 12,361	$ (2,763)
Operating expenses			
Research and development	52,255	34,425	17,830
General and administrative	24,322	14,060	10,262
Total operating expenses	76,577	48,485	28,092
Loss from operations	(66,979)	(36,124)	(30,855)
Other income (expense)			
Interest income	148	236	(88)
Interest expense	(8)	(20)	12
Change in fair value of equity securities	—	(733)	733
Change in fair value of the MSKCC success payments liability	(1,426)	—	(1,426)
Gain on extinguishment of the PPP Loan	1,584	—	1,584
Other income	79	514	(435)
Total other income (expense)	377	(3)	380
Net loss before provision for (benefit from) income taxes	(66,602)	(36,127)	(30,475)
Provision for (benefit from) income taxes	321	(1,819)	2,140
Net loss	$ (66,923)	$ (34,308)	$ (32,615)

Licensing and Collaboration Revenue

Licensing and collaboration revenue decreased $2.8 million, to $9.6 million for the year ended December 31, 2021 from $12.4 million for the year ended December 31, 2020. This decrease was primarily due to decreases of $7.5 million in revenue from a private company related party, and $0.8 million in revenue from Genus. These decreases were partially offset by a $4.0 million increase in revenue recognized under the AbbVie Agreement, and the remaining increase was primarily related to other license agreements with various licensees.

The following table summarizes our revenue by licensee for the years ended December 31, 2021 and 2020:

	Years Ended December 31,		
	2021	2020	Change
		(in thousands)	
AbbVie	$ 3,972	$ —	$ 3,972
Genus	—	844	(844)
Private company, related party	—	7,500	(7,500)
Pioneer, related party(1)	—	(250)	250
Other licensees	5,626	4,267	1,359
Total licensing revenue	$ 9,598	$ 12,361	$ (2,763)

(1) Includes the upfront payment to Pioneer for assignment of the chRDNA patent family.

Research and Development Expenses

Research and development expenses increased $17.8 million to $52.3 million for the year ended December 31, 2021 from $34.4 million for the year ended December 31, 2020. This increase was primarily related to increases of $10.1 million in external clinical trial-related activities and contract manufacturing activities for our product candidates, $4.8 million in other research and development expenses, $4.6 million in personnel-related expenses due to incremental hiring (which includes an increase in stock-based compensation expense of $0.6 million), and $1.3 million in facilities and other allocated expenses. These increases were partially offset by a $3.0 million decrease in expenses related to licenses, sublicensing revenue, and milestones.

General and Administrative Expenses

General and administrative expenses increased $10.2 million to $24.3 million for the year ended December 31, 2021 from $14.1 million for the year ended December 31, 2020. This increase was primarily related to increases of $4.3 million in personnel-related costs (which includes stock-based compensation expense increase of $1.8 million), $1.6 million in expenses related to accounting and financial services as part of being a public company in 2021, $1.5 million in recruiting costs, $1.3 million in insurance costs, and $1.3 million in facilities and other allocated expenses.

Total Other Income (Expense)

Total other income (expense) increased by $0.4 million for the year ended December 31, 2021 as compared to the year ended December 31, 2020.

We recognized expense related to the change in the fair value of the success payments liability under the MSKCC Agreement in the amount of $1.4 million for the year ended December 31, 2021. The MSKCC Agreement was entered into on November 13, 2020, and no similar expense was recorded during the year ended December 31, 2020.

Our PPP Loan was forgiven in May 2021, and we recognized a gain on the loan extinguishment of $1.6 million during the year ended December 31, 2021. No such gain was recognized for the year ended December 31, 2020.

We recognized a $0.7 million change in the fair value of our equity investment in Intellia common stock during the year ended December 31, 2020. We sold shares of Intellia common stock in 2020, and there were no changes in fair value of other equity securities during the year ended December 31, 2021. We have not owned any shares of Intellia common stock since March 31, 2020.

We recognized a $0.4 million change in other income (expense) during the year ended December 31, 2021 compared to December 31, 2020. The change primarily relates to the $0.5 million sale of certain of our patents and patent applications in the year ended December 31, 2020, which was not an ordinary business activity. No such sale occurred during the year ended December 31, 2021.

Income Tax

An income tax expense of $0.3 million was recognized for the year ended December 31, 2021, which was primarily related to state minimum taxes and an increase in the valuation allowance. An income tax benefit of $1.8 million was recognized for the year ended December 31, 2020, which was due primarily to the recognition of net operating loss carrybacks under the CARES Act, which generated a refund of taxes paid for the year ended December 31, 2018.

Liquidity, Capital Resources, and Capital Requirements

Sources of Liquidity

Since our inception, we have not generated any revenue from product sales and have incurred significant operating losses and negative cash flows from our operations. We have funded our operations through sales of our convertible preferred stock, which generated approximately $150.1 million in aggregate net proceeds, and from our IPO, which generated approximately $321.0 million in net proceeds. We have also received approximately $88.4 million in net proceeds from the sale of Intellia common stock that we received under the Intellia Agreement. Additionally, through December 31, 2021, we received approximately $75.2 million from licensing agreements, licensing and collaboration agreements, a service agreement, patent assignments, and government grants, including $30.2 million that was received from AbbVie under the AbbVie Agreement.

As of December 31, 2021, we had cash, cash equivalents, and marketable securities of $413.5 million. Based on our current operating plan, we expect that our existing cash, cash equivalents, and marketable securities will be sufficient to fund our current operating plan for at least the next 12 months from the date of this Annual Report on Form 10-K. We have based these estimates on our current assumptions, which may require future adjustments based on our ongoing business decisions. Because of the numerous risks and uncertainties associated with therapeutic product development, we may never achieve profitability and, unless and until we are able to develop and commercialize our product candidates, we will continue to be dependent upon equity financing, debt financing, and other forms of capital raises at least until we are able to generate significant positive cash flows from our operations, if ever.

Contractual Obligations and Commitments

We enter into contracts in the normal course of business with suppliers, CMOs, CROs, clinical trial sites, and the like. These agreements provide for termination at the request of either party generally with less than one-year notice and, therefore, we believe that our non-cancelable obligations under these agreements are not material. We do not currently expect any of these agreements to be terminated and do not have any non-cancelable obligations under these agreements as of December 31, 2021.

We have milestones, royalties, and/or other payments due to third parties under our existing license and assignment agreements. See Note 9 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K. We cannot estimate when such payments will be due and none of these events is probable to occur as of December 31, 2021.

MSKCC Agreement Success Payments

Under the MSKCC Agreement, we are obligated to make success payments to MSKCC of up to $35.0 million if our stock price increases by certain multiples of increasing value based on a comparison of the fair market value of our common stock with $5.1914 per share, adjusted for future stock splits, during a specified time period. As of December 31, 2021, the timing and likelihood of triggering the MSKCC success payments are uncertain. See Note 4 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for more information about the MSKCC success payments liability.

Leases

We lease laboratory and office space under non-cancellable operating agreements. On March 31, 2021, we entered into a ten-year lease agreement, which superseded and replaced our prior lease, as amended, and the new lease included additional office and laboratory space located within the same building in Berkeley, California. This lease agreement contains a renewal option for an additional term of five years. Monthly base rent under our lease agreements amounts to $0.3 million, subject to annual escalation from 3.1% to 3.5%. In addition to base rent, we pay our share of operating expenses and taxes. Our rent commitments under these leases are $3.5 million within the next 12 months from December 31, 2021, and $38.3 million for the remainder of the lease terms.

We entered into a new lease agreement with a commencement date of January 13, 2022, for an additional 10,000 square feet of laboratory and office space located in Berkeley, California. We have the option to extend the lease for five years. Our monthly base rent amounts to $0.1 million, subject to annual escalation of 3.5% with a total minimum lease payment of $9.2 million.

Funding Requirements

Our primary use of cash is to fund operating expenses and research and development expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable, accrued expenses, and prepaid expenses.

Our future funding requirements will depend on many factors, including the following:

- the initiation, progress, timing, costs, and results of preclinical studies and clinical trials for our product candidates;
- the clinical development plans we establish for these product candidates;
- the number and characteristics of the product candidates that we develop;
- the increase in the number of our employees and expansion of our physical facilities to support growth initiatives;
- the outcome, timing, and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities;
- whether we enter into any additional collaboration agreements and the terms of any such agreements;
- the cost of filing and prosecuting our patent applications, and maintaining and enforcing our patents and other intellectual property rights;
- the extent to which we acquire or in-license other product candidates and technologies;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against our products when we file for regulatory approval or thereafter;
- the effect of competing technological and market developments;
- the cost and timing of completion of commercial-scale outsourced manufacturing activities or the cost and timing of completion of clinical-scale and commercial-scale internal manufacturing activities;
- the cost of establishing sales, marketing, and distribution capabilities for any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products without a partner;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the achievement of milestones or occurrence of other developments that trigger payments by or to third parties under any collaboration or licensing agreements;
- our implementation of various computerized informational systems and efforts to enhance operational systems;
- the impact of the COVID-19 pandemic on our clinical development or operations; and
- the costs associated with being a public company.

Furthermore, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development expenditures.

If we need to raise additional capital to fund our operations, funding may not be available to us on acceptable terms, or at all. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of, or suspend one or more of our preclinical studies, clinical trials, research and development programs, and/or commercialization efforts. We may seek to raise any necessary additional capital through a combination of public or private equity offerings, debt financings, collaborations, and licensing arrangements. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in dilution to our stockholders. If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams, or research programs or grant licenses on terms that may not be favorable to us.

Cash Flows

Comparison of the Years Ended December 31, 2021 and 2020

The following summarizes our cash flows for the periods indicated:

	Years Ended December 31,		
	2021	2020	Change
	(in thousands)		
Cash used in operating activities	$ (32,519)	$ (33,215)	$ 696
Cash provided by (used in) investing activities	(176,397)	6,363	(182,760)
Cash provided by financing activities	433,429	1,735	431,694
Net increase (decrease) in cash and cash equivalents	$ 224,513	$ (25,117)	$ 249,630

Cash Used in Operating Activities

Net cash used in operating activities was $32.5 million and $33.2 million for the years ended December 31, 2021 and 2020, respectively.

Cash used in operating activities in the year ended December 31, 2021 was primarily due to our net loss of $66.9 million, adjusted by non-cash charges of $5.3 million and net changes in our net operating assets and liabilities of $29.1 million. Our non-cash charges were primarily comprised of $3.4 million of stock-based compensation, $1.4 million related to the change in the fair value of the MSKCC success payments liability, and $1.0 million of depreciation and amortization expense, which were offset by a gain of $1.6 million from the PPP Loan extinguishment upon the loan forgiveness. Acquired in-process research and development of $1.0 million consists of cash consideration reported in our investing activities. The changes in our net operating assets and liabilities were due to increases of $29.6 million in deferred revenue primarily from the upfront payment received from AbbVie, $4.3 million in accrued expenses and other current liabilities, $1.2 million in deferred rent and lease incentive liability, $1.1 million in accounts payable, $0.3 million in deferred tax liabilities, offset by increases of $4.0 million in prepaid expenses and other current assets, $1.8 million in other receivables, $1.0 million in accounts receivable, and $0.2 million in contract assets.

Cash used in operating activities in the year ended December 31, 2020 was primarily due to our net loss for the period of $34.3 million adjusted by non-cash charges of $0.9 million and net changes in our net operating assets and liabilities of $0.2 million. Our non-cash charges included $2.7 million for the fair value of the MSKCC success payments liability, $1.0 million of stock-based compensation expense, $0.9 million of depreciation expense, and $0.8 million of change in fair value of equity securities. These expenses were offset by $7.6 million of non-cash consideration for licensing and collaboration revenue. Acquired in-process research and development of $3.1 million includes $2.1 million of non-cash consideration and $1.0 million of cash consideration reported in our investing activities. The changes in our net operating assets and liabilities were primarily due to an increase of $2.3 million in accrued expenses and other current liabilities and a decrease of $0.4 million in prepaid expenses and other current assets, partially offset by an increase of $0.5 million in contract assets, an increase of $0.5 million in other receivables, a decrease of $0.6 million in deferred revenue, and a decrease of $0.5 million in deferred tax liabilities.

Cash Provided by (Used in) Investing Activities

During the year ended December 31, 2021, cash used in investing activities was $176.4 million. During the year ended December 31, 2020, cash provided by investing activities was $6.4 million.

Cash used in investing activities for the year ended December 31, 2021 was primarily due to our purchases of marketable securities of $173.3 million, purchases of property and equipment of $2.1 million, and payments to acquire in-process research and development of $1.0 million.

Cash provided by investing activities for the year ended December 31, 2020 was primarily due to the receipt of $7.7 million in proceeds from the sale of Intellia common stock. This was partially offset by cash paid for the acquisition of in-process research and development of $1.0 million and purchases of property and equipment of $0.3 million.

Cash Provided by Financing Activities

During the years ended December 31, 2021 and 2020, cash provided by financing activities was $433.4 million and $1.7 million, respectively.

Cash provided by financing activities for the year ended December 31, 2021 was primarily due to the receipt of net proceeds from our IPO in the amount of $321.0 million, net proceeds from the issuance of Series C convertible preferred stock in the amount of $108.8 million, proceeds from the exercise of stock options of $2.6 million, and repayment of the promissory note issued to our president and chief executive officer in the amount of $1.2 million, partially offset by principal payments for a capital lease of $0.1 million.

Cash provided by financing activities for the year ended December 31, 2020 was primarily due to our receipt of proceeds from our PPP Loan in the amount of $1.6 million and receipt of proceeds from exercise of stock options of $0.3 million, partially offset by principal payments for a capital lease of $0.1 million.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles ("U.S. GAAP"). The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. These estimates and assumptions are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates and assumptions could occur in the future. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ from these estimates under different assumptions or conditions.

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

Revenue Recognition

We recognize revenue when a licensee or assignee, or a customer, obtains control of the promised goods or services (e.g., an intellectual property license), in an amount that reflects the consideration that we have received or expect to receive in exchange for those goods or services.

We apply judgment to determine whether agreements are within the scope of revenue for customers or other accounting guidance at an agreement's effective date. Our revenues are primarily derived through our license agreements and license and collaboration agreements. The terms of these types of agreements may include (i) licenses for our technology, (ii) research and development services, and (iii) services or obligations in connection with participation in research or governance committees. Payments to us under these arrangements typically include one or more of the following: nonrefundable upfront license or exclusivity fees; annual maintenance fees; regulatory and/or commercial milestone payments; research and development payments; and royalties on the net sales of licensed products and/or services.

We assess whether the promises in our arrangements with customers are considered as distinct performance obligations that should be accounted for separately. Judgment is required to determine whether the license to intellectual property is distinct from the research and development services or participation on steering committees.

If the license to intellectual property controlled by us is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues allocated to the license at the point in time when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are combined with other promises, we utilize our judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Certain of our license agreements have two performance obligations: a license and a material right for annual license renewals. Such license agreements require payments of non-refundable annual license fees by the licensees (referred to as maintenance fees in the license agreements), which are accounted for as material rights for license renewals. We recognize revenue when the license is delivered and the term commences. Revenue for the material right for license renewals is recognized at the point in time the annual license fee is paid by the licensee and the renewal period begins.

Our collaboration and license agreements may include contingent milestone payments. Such milestone payments are typically payable when the collaboration partner or licensee achieves certain predetermined clinical, regulatory, and/or commercial milestones. Milestone payments that are not within our or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At each reporting date, we re-evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price by using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price in such period of determination.

Our collaboration and license agreements may also include contingent payments related to sales-based milestones. Sales-based milestones are typically payable when annual sales of a covered product reach specified levels. Sales-based milestones are recognized at the later of when the associated performance obligation has been satisfied or when the sales occur. Unlike other contingency payments, such as regulatory milestones, sales-based milestones are not included in the transaction price based on estimates at the inception of the contract, but rather, are included when the sales or usage occur.

Research and Development Expenses and Accrued Liabilities

As part of the process of preparing our financial statements, we are required to estimate and accrue expenses. Research and development expenses are charged to expense as incurred. Research and development expenses include certain payroll and personnel expenses; laboratory supplies; consulting costs; external clinical research and development expenses; and allocated overhead, including rent, equipment depreciation, and utilities.

We record accrued liabilities for estimated costs of research and development activities conducted by third-party service providers, CROs, and CMOs. We accrue for these costs based on factors such as estimates of the work completed and in accordance with service agreements established with these third-party service providers.

We make significant judgments and estimates in determining the accrual balance in each reporting period. As actual costs become known, we adjust our accruals. Although we do not expect our estimates to be materially different than the actual amounts incurred, the estimates for the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low in any one period. Our accrual is dependent, in part, upon the receipt of timely and accurate reporting from CROs, CMOs, and other third-party vendors. Variations in the assumptions used to estimate accruals including, but not limited to, the number of patients enrolled, the rate of patient enrollment and the actual services performed, may vary from our estimates, resulting in adjustments to clinical trial expenses in future periods. Changes in these estimates that result in material changes to our accruals could materially affect our financial condition and results of operations.

Stock-Based Compensation Expense

Stock-based compensation expense related to awards to employees is measured at the grant date based on the fair value of the award. The fair value of the award that is ultimately expected to vest is recognized as expense on a straight-line basis over the requisite service period of the awards, which is generally the vesting period, and is adjusted for pre-vesting forfeitures in the period in which the forfeitures occur.

We use the Black-Scholes valuation model as the method for determining the estimated fair market value of stock options and stock purchases under our 2021 Employee Stock Purchase Plan ("2021 ESPP") with the following assumptions:

Fair Market Value of Common Stock — Prior to our IPO, the fair market value of our common stock was determined by our board of directors with assistance from management and external valuation experts. Our approach to estimating the fair market value of our common stock was consistent with the methods outlined in the American Institute of Certified Public Accountants' Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Following our IPO, the fair market value of our common stock is based on its closing price on Nasdaq as reported on the date of the stock option grant.

Expected Term — Expected term represents the period that our stock-based awards are expected to be outstanding and is determined using the simplified method. The expected term for our 2021 ESPP is the offering period.

Expected Volatility — Expected volatility is estimated based on the average historical volatilities of common stock of comparable publicly traded entities over a period equal to the expected term of the stock option grants, as we do not have sufficient trading history for our common stock. Comparable companies are chosen based on their size, stage in the life cycle, or area of specialty. We will continue to apply this process for stock options awards and 2021 ESPP stock purchases until enough historical information regarding the volatility of our stock price becomes available.

Expected Dividends — Expected dividends is zero as we have never paid dividends on our common stock and have no plans to do so in the foreseeable future.

Risk-Free Interest Rate — Risk-free interest rate is based on the U.S. Treasury zero-coupon issued in effect at the time of grant for periods corresponding with the expected term of the award.

Stock-based compensation expense related to awards to non-employees, such as consultants, is recognized based on the then-current fair value at each grant date over the associated service period of the award, which is generally the vesting term, using the straight-line method. The fair value of non-employee stock options is estimated using the Black-Scholes valuation model with assumptions generally consistent with those used for employee stock options, with the exception of the expected term, which is the remaining contractual life at each measurement date. See Note 12 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for more information on assumptions used in estimated stock-based compensation expense.

We recorded stock-based compensation expense of $3.5 million and $1.0 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, there was $34.5 million of total unrecognized compensation expense, which we expect to recognize over a remaining weighted-average period of 3.1 years. We expect to continue to grant equity-based awards in the future, and to the extent that we do, our stock-based compensation expense recognized in future periods will likely increase.

MSKCC Success Payments Liability

Under the MSKCC Agreement, we are obligated to make success payments and a change of control payment to MSKCC of up to $35.0 million, as discussed above. The liability associated with these potential success payments is accounted for at fair value as a long-term liability. The MSKCC success payments liability is estimated at fair value at inception and at each subsequent balance sheet date, and changes in the fair value of the liability are recognized as expense or income as part of "other income (expense)" in our consolidated statements of operations and comprehensive loss until the success payments liability is paid or expires. We estimated the fair value of the success payments liability to be equal to $4.1 million and $2.7 million as of December 31, 2021 and 2020, respectively. Change in the fair value of the MSKCC success payments liability of $1.4 million was recognized in other income (expense) for the year ended December 31, 2021. We recognized $2.7 million in research and development expense related to the initial fair value of the MSKCC success payments liability for the year ended December 31, 2020. Change in the fair value of the success payments liability was insignificant for the year ended December 31, 2020.

To determine the estimated fair value of the MSKCC success payments liability, we use a Monte Carlo simulation methodology, which models the future movement of our stock price based on several key variables. The following variables were incorporated in the estimated fair value of the success payments liability: estimated term of the success payments, fair value of common stock, expected volatility, risk-free interest rate, and estimated number and timing of valuation measurement dates on the basis of which payments may be triggered. The computation of expected volatility was estimated using a combination of available information about the historical volatility of stocks of similar publicly traded companies for a period matching the expected term assumption and its historical and projected volatility. There are several valuation measurement dates that will occur subsequent to the filing of this Annual Report on Form 10-K, on the basis of which payments may be triggered.

Income Taxes

We account for income taxes using the asset and liability method. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in our consolidated financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax.

Recently Issued Accounting Pronouncements

See Note 2 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for more information regarding recently issued accounting pronouncements.

Indemnification Agreements

As permitted under Delaware General Corporation Law and in accordance with our amended and restated bylaws, we indemnify our executive officers and directors for certain events or occurrences while they are or were serving in that capacity. We are also party to indemnification agreements with our executive officers, directors, and vice-president and controller. We believe the fair value of the indemnification rights and agreements is minimal. Accordingly, we have not recorded any liabilities for these indemnification rights and agreements as of December 31, 2021.

Emerging Growth Company Status

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

We expect to use the extended transition period for any other new or revised accounting standards during the period in which we remain an emerging growth company. As described in *Recent Accounting Pronouncements* in Note 2 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we have early adopted multiple accounting standards, because the JOBS Act does not preclude an emerging growth company from adopting a new or revised accounting standard earlier than the time that such standard applies to private companies, to the extent early adoption is allowed by the accounting standard.

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

We had cash, cash equivalents, and marketable securities of $413.5 million as of December 31, 2021, consisting of cash, money market funds, government securities, commercial paper, and corporate bonds, and we had cash and cash equivalents of $16.0 million as of December 31, 2020, consisting of cash and money market funds. To date, fluctuations in interest income have not been significant.

We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate risk exposure. A hypothetical 10% change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements. We have not been exposed to, nor do we anticipate being exposed to, material risks due to changes in interest rates.

We do not have any foreign currency. Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our results of operations during the year ended December 31, 2021.

Item 8. Financial Statements and Supplementary Data.

The information required by this item is presented at the end of this Annual Report on Form 10-K beginning on page F-1. An index of those financial statements is found in Part IV, Item 15, *Exhibits, Financial Statement Schedules*, of this Annual Report on Form 10-K.

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

None

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We have established disclosure controls and procedures designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms and is accumulated and communicated to management, including the principal executive officer (our president and chief executive officer) and principal financial officer (our chief financial officer), to allow timely decisions regarding required disclosure.

Our management, under the supervision and with the participation of our president and chief executive officer and chief financial officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K.

Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs. Based on such evaluation, our president and chief executive officer and our chief financial officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2021.

Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management’s assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by the rules of the Securities and Exchange Commission for newly public companies.

Changes in Internal Control

There were no changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a-15(f) or 15d-15(f) of the Exchange Act during our fourth fiscal quarter ended December 31, 2021 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Not applicable.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Board of Directors

Our board of directors ("Board") is comprised of three classes, with members holding office for three-year terms. There are currently seven directors on our Board. Set forth below are the names, ages, and certain other information about each member as of March 17, 2022. There are no family relationships among any of our directors and executive officers, and no arrangement or understanding exists between any director and any other person pursuant to which any director was selected to serve on our Board.

Name	Age	Position	Class
Andrew Guggenhime, M.B.A.(1)(2)	53	Director (Chair)	Class II
Scott Braunstein, M.D.(1)(2)	58	Director	Class I
Rachel Haurwitz, Ph.D.	36	Director, president and chief executive officer	Class III
Dara Richardson-Heron, M.D.(3)	58	Director	Class III
Natalie Sacks, M.D.(1)(3)(4)	57	Director	Class III
Nancy Whiting, Pharm.D.(2)(4)	49	Director	Class II
Ran Zheng(3)(4)	58	Director	Class I

(1) Member of the Audit Committee
(2) Member of the Compensation Committee
(3) Member of the Nominating and Corporate Governance Committee
(4) Member of the Science and Technology Committee

Andrew Guggenhime, M.B.A., has served on our Board since April 2021. Mr. Guggenhime currently serves as President and Chief Financial Officer at Vaxcyte, Inc. ("Vaxcyte"), a developer of vaccines, positions he has held since January 2021. He served as Chief Operating Officer and Chief Financial Officer of Vaxcyte from May 2020 to December 2020. Prior to joining Vaxcyte, he served as Chief Financial Officer of Dermira, Inc. ("Dermira"), a biopharmaceutical company, from April 2014 through the acquisition of the company by Eli Lilly and Company in February 2020. Prior to Dermira, Mr. Guggenhime served as Chief Financial Officer for CardioDx, Inc., a medical diagnostic company, from September 2011 to April 2014 and as a director of the company from April 2014 to July 2016. He also served as Chief Financial Officer for Calistoga Pharmaceuticals, Inc., a biopharmaceutical company, from September 2010 to April 2011, which was acquired by Gilead Sciences, Inc. in 2011, and as Chief Financial Officer for Facet Biotech Corporation ("Facet Biotech"), a biotechnology company, from December 2008 to June 2010, which was acquired by Abbott Laboratories in April 2010. Mr. Guggenhime previously served as Chief Financial Officer of PDL BioPharma, Inc. ("PDL BioPharma"), a biopharmaceutical company, until Facet Biotech was spun off from PDL BioPharma in December 2008. Prior to joining Facet Biotech, he served as Chief Financial Officer for Neoforma, Inc., a provider of supply chain management solutions, which was acquired by Global Healthcare Exchange, LLC in March 2006. Mr. Guggenhime began his career in financial services at Merrill Lynch & Co. and Wells Fargo & Company. He received his B.A. in International Politics and Economics from Middlebury College and his M.B.A. from the J.L. Kellogg Graduate School of Management at Northwestern University. Since July 2018, Mr. Guggenhime has served on the Board of Directors of Metacrine, Inc., where he is Chair of the Audit Committee. We believe that Mr. Guggenhime is qualified to serve on our Board based on his more than two decades of finance, strategic, and operational leadership experience at both private and public healthcare companies.

Scott Braunstein, M.D., has served on our Board since June 2021. Dr. Braunstein currently serves as President and Chief Executive Officer and a member of the Board of Directors of Marinus Pharmaceuticals, Inc., positions he has held since August 2019 and September 2018, respectively. Since August 2015, he has served as an operating partner at Aisling Capital, an investment firm. From July 2015 to March 2018, Dr. Braunstein served as Chief Strategy Officer and Chief Operating Officer at Pacira Pharmaceuticals, Inc. ("Pacira"), a pharmaceutical company. Prior to Pacira, Dr. Braunstein served as a healthcare portfolio manager at Everpoint Asset Management from September 2014 to February 2015 and spent 12 years from February 2002 to June 2014 with J.P. Morgan Asset Management as a healthcare analyst and managing director on the U.S. equity team and as portfolio manager of the J.P. Morgan Global Healthcare Fund. He previously served on the Board of Directors of Constellation Pharmaceuticals from February 2019 to July 2021 (where he served as Chair of the Audit Committee); of Ziopharm Oncology, Inc. from September 2018 to November 2020; of Esperion Therapeutics, Inc. from June 2015 to April 2020 (where he served as Chair of the Audit Committee); and of Protara Therapeutics, Inc. from May 2018 to July 2020 (where he served on the Audit Committee). Dr. Braunstein began his career as a physician at the Summit Medical Group and as assistant clinical professor at Albert Einstein College of Medicine and Columbia University Medical Center. He received his B.S. in Biology from Cornell University and his M.D. from the Albert Einstein College of

Medicine. Since September 2018, Dr. Braunstein has served on the Board of Directors of Trevena, Inc., a biopharmaceutical company, where he is a member of the Audit Committee. We believe that Dr. Braunstein is qualified to serve on our Board based on his expertise and experience in governing, leading, and investing in biopharmaceutical companies.

Rachel Haurwitz, Ph.D., is a co-founder of Caribou and has served as our President and Chief Executive Officer and a director of our company since its inception in October 2011. Dr. Haurwitz is an inventor on patents and patent applications covering multiple CRISPR-based technologies and has co-authored several scientific papers characterizing CRISPR-Cas systems including in *Science*. From July 2014 until November 2016, Dr. Haurwitz served on the Board of Directors of Intellia Therapeutics, Inc., of which she is a co-founder. She received her A.B. degree in Biological Sciences from Harvard College. Dr. Haurwitz received her Ph.D. in Molecular and Cell Biology from the University of California, Berkeley, where she completed her thesis research in the laboratory of Dr. Jennifer A. Doudna. Since November 2021, Dr. Haurwitz has served on the Board of Directors of Seer, Inc. and since February 2020, Dr. Haurwitz has served on the Board of Directors of the Biotechnology Industry Organization, a not-for-profit organization. We believe that Dr. Haurwitz is qualified to serve on our Board based on her operational and historical expertise and experience as a co-founder, President and Chief Executive Officer of our company, and member of our Board, combined with her knowledge of CRISPR technology.

Dara Richardson-Heron, M.D., has served on our Board since November 2021. She is the Chief Executive Officer of DRH Consulting, a management and executive consulting firm, a position she has held since August 2021. Dr. Richardson-Heron recently served as Chief Patient Officer for Pfizer, Inc., a biopharmaceutical company, from February 2020 to August 2021. Her previous executive leadership positions include Chief Engagement Officer and Scientific Executive for National Institutes of Health (March 2017 to January 2020); Chief Executive Officer of YWCA USA, Inc. (2012 to 2017); and Chief Executive Officer, Greater NYC Affiliate of Susan G. Komen for the Cure (2008 to 2012). Earlier in her career, she served as Assistant Executive Director/National Chief Medical Officer with United Cerebral Palsy of NYC/UCP Association and Executive Medical Director and Special Assistant to the Chairman and Chief Executive Officer at Consolidated Edison Company of New York, Inc. Dr. Richardson-Heron holds a B.A. in Biology from Barnard College and an M.D. from New York University School of Medicine. We believe Dr. Richardson-Heron is qualified to serve on our Board based on her executive leadership expertise and her experience representing the perspective of patients.

Natalie Sacks, M.D., has served on our Board since May 2018. Dr. Sacks is an oncologist and experienced drug developer. She has been the Chief Medical Officer at Harpoon Therapeutics, Inc. since October 2018. Prior to joining Harpoon, Dr. Sacks held various development leadership roles at multiple companies including Onyx Pharmaceuticals Inc., a pharmaceutical company (acquired by Amgen Inc. in 2013), from April 2011 to February 2014; Aduro Biotech, Inc., a clinical stage biopharmaceutical company, from September 2016 to September 2018; Exelixis, Inc., a pharmaceuticals company, from September 2009 to March 2011; and Cell Genesys, Inc., a biotechnology company, from November 2002 to April 2009. She has been responsible for all aspects of development, including the late-stage development of Kyprolis®, a therapeutic for treating multiple myeloma developed by Onyx Pharmaceuticals Inc., and Cometriq®, a therapeutic for treating metastatic medullary thyroid cancer developed by Exelixis, Inc. From October 2004 to October 2016, Dr. Sacks held a faculty appointment at the University of California, San Francisco, where she was a volunteer assistant clinical professor of medicine in the Division of Hematology/Oncology. She received her B.A. in Mathematics from Bryn Mawr College, her M.S. in Biostatistics from Harvard University School of Public Health, and her M.D. from the University of Pennsylvania School of Medicine. Since August 2017, Dr. Sacks has served on the Board of Directors of Zymeworks, Inc., a clinical stage biotechnology company. We believe that Dr. Sacks is qualified to serve on our Board based on her extensive experience developing late-stage oncology therapeutics and her experience serving as a director of a public company and in executive leadership roles at multiple companies.

Nancy Whiting, Pharm.D., has served on our Board since August 2021. Dr. Whiting is the Chief Executive Officer and a member of the Board of Directors at Recludix Pharma, a biotechnology company, where she has served since September 2021. She spent almost 15 years (from 2007 to 2021) with Seagen Inc., a biotechnology company (formerly Seattle Genetics), where she most recently served as Executive Vice President of Corporate Strategy. Dr. Whiting previously served as Executive Vice President of Late-Stage Development, Senior Vice President of Clinical Development and Medical Affairs, and Head of Experimental Medicine at Seagen. Prior to her tenure in the biopharmaceutical industry, she had a career in clinical pharmacy serving as a Clinical Oncology Pharmacist at Seattle Cancer Care Alliance, and previously as the Staff Pharmacist for the Bone Marrow Transplant and Acute Leukemia department at Vancouver Hospital. Dr. Whiting received a B.S. in Pharmacy from the University of British Columbia and earned her Pharm.D. degree from the University of Washington. We believe Dr. Whiting is qualified to serve on our Board based on her extensive experience in all phases of drug development.

Ran Zheng has served on our Board since September 2021. Ms. Zheng has served as Chief Executive Officer and on the Board of Directors of Landmark Bio, a public benefit limited liability company to advance the development of transformative new medicines, since March 2021. Prior to joining Landmark Bio, Ms. Zheng most recently served as Chief Technical Officer at Orchard Therapeutics, a commercial-stage global gene therapy, from March 2019 to February 2021. In that role, Ms. Zheng led the technical

operations organization and helped advance the company's product pipeline. Ms. Zheng has also held leadership positions at multiple biotechnology companies, including Amgen Inc., a biopharmaceutical company, from 2003 to 2010, and Genzyme, a biotechnology company (now Sanofi), from 1996 to 2000. Ms. Zheng holds a B.S. in Biology from Beijing Forestry University and received an M.S. in Microbial Engineering from the University of Minnesota. We believe Ms. Zheng is qualified to serve on our Board based on her extensive leadership experience in the biotechnology industry.

Classified Board of Directors

In accordance with our amended and restated certificate of incorporation, our Board is divided into three classes of directors. At each annual meeting of stockholders, a class of directors will be elected for a three-year term to succeed the class whose terms are then expiring, to serve from the time of election and qualification until the third annual meeting following their election or until their earlier death, resignation, or removal. Our directors are divided among the three classes as follows:

The Class I directors are Dr. Braunstein and Ms. Zheng, whose terms will expire at our 2022 annual meeting of stockholders.

The Class II directors are Mr. Guggenhime and Dr. Whiting, whose terms will expire at our 2023 annual meeting of stockholders.

The Class III directors are Dr. Haurwitz, Dr. Richardson-Heron, and Dr. Sacks, whose terms will expire at our 2024 annual meeting of stockholders.

Our amended and restated certificate of incorporation provides that the authorized number of directors may be changed only by resolution of our Board. The division of our Board into three classes with staggered three-year terms may delay or prevent a change in control. See *Risk Factors - "Provisions in our amended and restated certificate of incorporation, our amended and restated bylaws, and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management,"* in Part I, Item 1A of this Annual Report on Form 10-K for a discussion of these and other anti-takeover provisions found in our amended and restated certificate of incorporation and amended and restated bylaws.

Director Independence

Under Nasdaq rules, independent directors must comprise a majority of a listed company's board of directors within one year of the completion of its initial public offering. In addition, Nasdaq rules require that, subject to specified exceptions, each member of a listed company's audit and compensation committees be independent and that director nominees be selected or recommended for the board's selection by independent directors constituting a majority of the independent directors or by a nominating and corporate governance committee comprised solely of independent directors. Under Nasdaq rules, a director will only qualify as "independent" 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 and that such person is "independent" as defined under applicable Nasdaq rules.

Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in their capacity as a member of the audit committee, the board of directors, or any other board committee: (i) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or (ii) be an affiliated person of the listed company or any of its subsidiaries.

Based upon information requested from and provided by each director concerning their background, employment, and affiliations, including family relationships, our Board has determined, with the assistance of counsel, that each of our directors, with the exception of Dr. Haurwitz, is an "independent director" as defined under applicable Nasdaq rules and that each member of the audit committee of our Board also meets the independence criteria set forth in Rule 10A-3 under the Exchange Act. Each of the members of our compensation committee is a "non-employee director" as defined in Section 16b-3 of the Exchange Act. In determining independence, our Board considered the relationships that each non-employee director has with our company and all other facts and circumstances that our Board deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director. Dr. Haurwitz is not an independent director under these rules because she is our president and chief executive officer.

Board Committees

Our Board has established an audit committee, a compensation committee, a nominating and corporate governance committee, and a science and technology committee, each of which operates pursuant to a charter adopted by our Board. The Board may also establish other committees from time to time to assist our management and Board in their duties. The composition and functioning of each of our board committees complies with all of the applicable requirements of the Sarbanes-Oxley Act, Nasdaq, and the Exchange Act. Each committee charter is available on the Corporate Governance section of our website, https://investor.cariboubio.com/investors. Information contained on our website is not incorporated by reference into this Annual Report on Form 10-K.

The members of the audit committee are Dr. Braunstein, Mr. Guggenhime (Chair), and Dr. Sacks. Our Board has determined that Mr. Guggenhime, who is an independent director, qualifies as an "audit committee financial expert," as defined under Item 407 of Regulation S-K.

Code of Business Conduct, Scientific and Data Integrity, and Ethics

We have adopted a written Code of Business Conduct, Scientific and Data Integrity, and Ethics ("Code of Conduct") that applies to all of our employees, consultants, contractors, and directors. A current copy of the Code of Conduct is available on the Corporate Governance section of our website, https://cariboubio.com/investors. The audit committee of our Board is responsible for overseeing the Code of Conduct and must approve any waivers of the Code of Conduct for our executive officers and directors. We expect that any amendments to the Code of Conduct, or any waivers of its requirements with respect to our executive officers and directors, will be disclosed on our website at the address indicated above. Our website and the information contained therein or connected thereto shall not be deemed to be incorporated into this Annual Report on Form 10-K. We have included our website address as an inactive textual reference only. We will provide to any person, without charge, a copy of the Code of Conduct. Any such request should be directed to Caribou Biosciences, Inc., 2929 7th Street, Suite 105, Berkeley, California 94710, Attn: Chief Legal Officer and Corporate Secretary, telephone: 510-982-6030.

Executive Officers

Our executive officers and their ages and positions as of March 17, 2022 are as set forth below. Our executive officers hold office at the discretion of the Board and until their successors shall have been duly elected and qualified, unless sooner removed. There are no family relationships among any of our executive officers and directors and no arrangement or understanding exists between any executive officer and any other person pursuant to which an executive offer was selected to serve.

Name	**Age**	**Position(s)**
Rachel E. Haurwitz, Ph.D.	36	President and chief executive officer; Director
Steven B. Kanner, Ph.D.	63	Chief scientific officer
Ruhi A. Khan, M.B.A.	47	Chief business officer
Barbara G. McClung, J.D.	67	Chief legal officer and corporate secretary
Jason V. O'Byrne, M.B.A.	53	Chief financial officer
Syed A. Rizvi, M.D.	55	Chief medical officer

Rachel E. Haurwitz, Ph.D., is a co-founder of Caribou and has served as our president and chief executive officer and a director of our company since its inception in October 2011. Dr. Haurwitz is an inventor on patents and patent applications covering multiple CRISPR-based technologies and has co-authored several scientific papers characterizing CRISPR-Cas systems including in *Science*. From July 2014 until November 2016, Dr. Haurwitz served on the Board of Directors of Intellia Therapeutics, Inc., of which she is a co-founder. She received her A.B. degree in Biological Sciences from Harvard College. Dr. Haurwitz received her Ph.D. in Molecular and Cell Biology from the University of California, Berkeley, where she completed her thesis research in the laboratory of Dr. Jennifer A. Doudna. Since November 2021, Dr. Haurwitz has served on the Board of Directors of Seer, Inc. and since February 2020, Dr. Haurwitz has served on the Board of Directors of the Biotechnology Industry Organization, a not-for-profit organization.

Steven B. Kanner, Ph.D., has served as our chief scientific officer since June 2017. Before joining Caribou, Dr. Kanner served as Vice President, Head of Biology at Arrowhead Pharmaceuticals, Inc. ("Arrowhead"), a pharmaceuticals company, from September 2013 to June 2017, leading a department in discovery of RNAi therapeutics for oncology, genetic diseases, and other indications. Prior to joining Arrowhead, he served in various positions of increasing responsibility in both oncology and inflammation drug discovery at Bristol-Myers Squibb, from July 1990 to May 2003; Agensys Corporation, a pharmaceuticals company (which was acquired by Astellas Pharma Inc. in 2007), from May 2003 to June 2010; and Astex Pharmaceuticals, Inc., from December 2010 to July 2012. Dr. Kanner has authored over 85 publications in both peer-reviewed journals and books and is an inventor on numerous U.S. and foreign patents and patent applications. He received his A.B. degree in Genetics from the University of California, Berkeley,

and his Ph.D. in Immunology and Microbiology from the University of Miami Miller School of Medicine. He was awarded an NIH post-doctoral fellowship that he completed at the University of Virginia.

Ruhi A. Khan, M.B.A., has served as our chief business officer since November 2021. She brings over 20 years of business development and investment management experience focused on the biotechnology and pharmaceutical industries. Most recently she served as head of business development at Tempest Therapeutics, Inc. and Adastra Pharmaceuticals, Inc., both biotechnology companies, from 2019 to 2021, and she provided business development and finance advice to multiple biotechnology companies from 2015 to 2021. From 2009 to 2014, she was the Vice President of Business Development for Acorda Therapeutics, Inc. ("Acorda"), a biotechnology company. Prior to Acorda, she worked in a similar capacity at Lexicon Pharmaceuticals, Inc., a pharmaceutical company. She started her career in venture capital with Fidelity Biosciences Group (now F-Prime Capital) and MPM Capital Advisors. Ms. Khan holds an A.B. in Biology from Harvard College and an M.B.A. in healthcare management from The Wharton School, University of Pennsylvania.

Barbara G. McClung, J.D., has served as our chief legal officer and corporate secretary since April 2015. Additionally, Ms. McClung currently teaches biotechnology law at the University of California, Berkeley, School of Law. Prior to joining Caribou, she was Vice President, General Counsel, and Corporate Secretary of Intarcia Therapeutics, Inc., from January 2007 to May 2013. Ms. McClung was Chief Legal Officer and Corporate Secretary at Cygnus, Inc., from January 1998 to December 2005. Ms. McClung began her career as a patent attorney with E. I. du Pont de Nemours and Company from May 1987 to May 1989, and then was an associate at the law firm of Townsend & Townsend from June 1989 to August 1990. Ms. McClung was Corporate Patent Counsel – Vaccines Division at Chiron Corporation from August 1990 to January 1998. Ms. McClung is a registered patent attorney before the United States Patent and Trademark Office. She received her B.A. in Anthropology from the University of California, San Diego, her M.A. in Anthropology from the University of Pennsylvania, and her J.D. from the University of Pennsylvania Law School, and she is a member of the California, Delaware, and Pennsylvania state bars.

Jason V. O'Byrne, M.B.A., has served as our chief financial officer since February 2021. Prior to joining Caribou, he was Senior Vice President of Finance at Audentes Therapeutics, Inc. ("Audentes"), a gene therapy company, from April 2020 to February 2021, where he led finance. From April 2019 to April 2020, Mr. O'Byrne served as Vice President of Finance at Audentes. Before joining Audentes, he spent 13 years with Genentech, Inc., a member of the Roche Group, from February 2005 to December 2018, holding finance leadership and executive positions across the research, development, manufacturing, business development, and commercial functions. Earlier in his career, Mr. O'Byrne served as regional controller with General Chemical Corporation, a specialty chemical supplier, from September 2002 to January 2005, and as an engineer with General Motors, from September 1999 to September 2001. He received a B.A.Sc. in Mechanical Engineering from the University of British Columbia, and an M.B.A. from New York University's Stern School of Business.

Syed A. Rizvi, M.D., has served as our chief medical officer since January 2022. From December 2020 to January 2022, he served as Chief Medical Officer at Chimeric Therapeutics Limited, a clinical stage cell therapy company, where he led the strategy and execution of clinical development programs for the company's T cell and NK cell therapy platforms. Previously, he was Vice President and Head of Clinical Development and Medical Affairs at Legend Biotech Corporation ("Legend") from June 2018 to November 2020. Prior to Legend, he was employed by Celgene Corporation (now a Bristol Myers Squibb company) from March 2014 to June 2018, where he was responsible for strategic direction and management of Celgene's CAR-T cell and immuno-oncology therapy portfolios. He earned his medical degree from Dow Medical College at Karachi University.

Delinquent Section 16(a) Reports

Our Section 16 officers, our directors, and persons who own beneficially more than 10% of our equity securities are required under Section 16(a) of the Securities Exchange Act of 1934 to file reports of ownership and changes in their ownership of our securities with the SEC. They must also furnish copies of these reports to us. Based solely on a review of the copies of reports furnished to us we believe that for our 2021 fiscal year our Section 16 officers and our directors complied with all applicable Section 16(a) filing requirements except that Ryan Fischesser, our vice president of finance and controller, inadvertently filed his Form 3 one day late.

Item 11. Executive Compensation.

The following discussion and analysis of compensation arrangements should be read with the compensation tables and related narratives and disclosures set forth below. This discussion contains forward-looking statements that are based on our current plans and expectations regarding future compensation programs. Actual compensation programs that we adopt may differ materially from the programs summarized in this discussion.

Introduction

This section provides an overview of the compensation awarded to, earned by, or paid to our principal executive officer and our next two most highly compensated executive officers in respect of their service to us for the fiscal year ended December 31, 2021. We refer to these individuals as our named executive officers. Our named executive officers are:

- Rachel E. Haurwitz, Ph.D., our president and chief executive officer;
- Jason V. O'Byrne, M.B.A, our chief financial officer; and
- Barbara G. McClung, J.D., our chief legal officer and corporate secretary.

Named Executive Officer Summary Compensation Table (2021 and 2020)

The following table sets forth the compensation awarded to, earned by, or paid to our named executive officers in respect of their service to us for the fiscal years ended December 31, 2021 and 2020 (as applicable):

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Option Awards ($)(3)	All Other Compensation ($)	Total ($)
Rachel E. Haurwitz, Ph.D.	2021	527,386	319,069	5,391,864	11,600 (4)	6,249,919
President and chief executive officer	2020	450,000	202,500	—	11,400	663,900
Jason V. O'Byrne, M.B.A.	2021	358,580	227,775 (2)	2,862,675	—	3,449,030
Chief financial officer	2020	—	—	—	—	—
Barbara G. McClung, J.D.	2021	414,432	182,350	2,134,672	11,600 (4)	2,743,054
Chief legal officer and corporate secretary	2020	365,000	127,750	—	11,400	504,150

(1) Except as indicated in footnote 2, the 2021 bonuses were paid in February 2022, and the 2020 bonuses were paid in February 2021.
(2) The 2021 bonus amount for Mr. O'Byrne includes an annual bonus of $157,775 paid in February 2022, plus a one-time contingent bonus of $70,000 paid in March 2021. See narrative disclosure below for details.
(3) The amounts shown represent the grant date fair values of option awards granted in 2021 as computed in accordance with Financial Accounting Standards Board (FASB) Accounting Standard Codification Topic 718 ("ASC Topic 718"). There were no option awards in 2020. See Note 12 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a discussion of the assumptions used in the calculation of these amounts.
(4) Consists of 401(k) retirement plan matching contributions for 2021 and 2020 of $11,600 and $11,400, respectively.

Narrative Disclosure to Named Executive Officer Summary Compensation Table

Our Board approves compensation for our named executive officers and other executive officers based, in part, upon recommendations of the Board's compensation committee.

Base Salary

Effective January 1, 2021, the base salaries for Dr. Haurwitz and Ms. McClung were $495,000 and $395,000, respectively. Mr. O'Byrne's base salary was $385,000 as of his February 8, 2021 hire date. Effective July 27, 2021, the base salaries for Dr. Haurwitz, Mr. O'Byrne, and Ms. McClung were increased to $570,000, $415,000, and $440,000, respectively. Amounts in the Named Executive Officer Summary Compensation Table are prorated for each salary level.

During fiscal year 2020 the base salaries for Dr. Haurwitz and Ms. McClung were $450,000 and $365,000, respectively.

Bonuses

Pursuant to the terms of their employment agreements, Dr. Haurwitz, Mr. O'Byrne and Ms. McClung were eligible to receive annual bonuses for fiscal years 2021, and Dr. Haurwitz and Ms. McClung were eligible to receive annual bonuses for 2020.

For fiscal year 2021, the target bonus amounts, expressed as a percentage of base salary paid, for Dr. Haurwitz, Mr. O'Byrne, and Ms. McClung were 55%, 40%, and 40%, respectively. Actual bonuses for fiscal year 2021, paid in February 2022, for Dr. Haurwitz, Mr. O'Byrne, and Ms. McClung were $319,069, $157,775, and $182,350, respectively, which reflected 110% of the target amounts. The final payout percentages were determined based on achievement of defined company goals in fiscal year 2021.

In addition, pursuant to his offer letter, in March 2021 we paid Mr. O'Byrne a one-time bonus of $70,000 that was contingent on both the closing of our Series C preferred stock financing (which occurred in March 2021) and Mr. O'Byrne not receiving a bonus for 2020 from his previous employer (which he did not). If, within one year from the date of the bonus payment, Mr. O'Byrne had chosen to leave our company or if his employment was terminated by us for cause, then Mr. O'Byrne would have been required to repay us a prorated portion of this bonus.

For fiscal year 2020, the target bonus amounts, expressed as a percentage of base salary paid, for Dr. Haurwitz and Ms. McClung were 45% and 35%, respectively. Actual bonuses for fiscal year 2020, paid in February 2021, for Dr. Haurwitz and Ms. McClung were $202,500 and $127,750, respectively, which reflected 100% of the target bonus amounts. The final payout percentages were determined based on achievement of defined company goals in fiscal year 2020.

Equity Compensation Awards

On March 30, 2021, Dr. Haurwitz and Ms. McClung were awarded stock options under the 2013 Equity Incentive Plan, as amended and restated (the "2013 Plan") covering 437,201 and 231,914 shares of our common stock, respectively, at an exercise price of $4.11 per share. For each option granted on March 30, 2021, 1/4th of the shares subject to the option vest on the one-year anniversary of the March 2, 2021 vesting commencement date and an additional 1/48th of the aggregate number of shares subject to the option vest on the corresponding day of each month thereafter, subject to each executive officer's continued service with us through the applicable vesting dates.

On March 30, 2021, Mr. O'Byrne was awarded stock options under the 2013 Plan covering 437,201 shares of our common stock at an exercise price of $4.11 per share. The option vested as to 1/4th of the shares on the one-year anniversary of February 8, 2021 (Mr. O'Byrne's hire date), and an additional 1/48th of the aggregate number of shares subject to the option will vest on the corresponding day of each month thereafter, subject to Mr. O'Byrne's continued service with us through the applicable vesting dates. On June 29, 2021, Mr. O'Byrne was awarded stock options under the 2013 Plan covering 48,966 shares of our common stock at an exercise price of $5.27 per share. The option will vest as to 1/4th of the shares on the one-year anniversary of the grant date and an additional 1/48th of the aggregate number of shares subject to the option will vest on the corresponding day of each month thereafter, subject to Mr. O'Byrne's continued service with us through the applicable vesting dates.

On December 20, 2021, Dr. Haurwitz, Mr. O'Byrne, and Ms. McClung were awarded stock options under the 2021 Equity Incentive Plan (the "2021 Plan") covering 411,00, 147,000, and 147,000 shares, respectively, at an exercise price of $15.16 per share. For each option granted on December 20, 2021, the shares vest in equal monthly installments (commencing January 20, 2022) over four years, subject to each executive officer's continued service to us through the applicable vesting dates.

We did not grant any stock options to Dr. Haurwitz or Ms. McClung in 2020.

Employment Agreements with Our Named Executive Officers

We have entered into written employment agreements with each of our executive officers, including each of our named executive officers, which employment agreements are described below.

Officer Employment Agreement with Dr. Haurwitz

On July 27, 2021, we entered into an officer employment agreement with Dr. Haurwitz setting forth the terms and conditions of her employment with us. The new agreement amended and restated a prior officer employment agreement dated June 30, 2017. The agreement provides for Dr. Haurwitz to serve as our president and chief executive officer. Under the terms of her agreement, Dr. Haurwitz's initial base salary was $570,000 and her initial target annual bonus opportunity was 55% of her annual base salary. Both of these amounts are subject to review and adjustment by the Board from time to time. Additional details about this agreement are provided in *Severance and Change of Control Payments and Benefits* below.

Officer Employment Agreement with Mr. O'Byrne

On July 27, 2021, we entered into an officer employment agreement with Mr. O'Byrne setting forth the terms and conditions of his employment with us. The new agreement amended and restated a prior officer employment agreement dated February 8, 2021. The employment agreement provides for Mr. O'Byrne to serve as our Chief Financial Officer. Under the terms of his agreement, Mr. O'Byrne's initial base salary was $415,000 and his initial target bonus opportunity was 40% of his annual base salary. Both of these amounts are subject to review and adjustment by the Board from time to time. Additional details about this agreement are provided in *Severance and Change in Control Payments and Benefits* below.

Officer Employment Agreement with Ms. McClung

On July 27, 2021, we entered into an officer employment agreement with Ms. McClung setting forth the terms and conditions of her employment with us. The new agreement amended and restated a prior officer employment agreement dated June 30, 2017. The agreement provides for Ms. McClung to serve as our chief legal officer and corporate secretary. Under the terms of her agreement, Ms. McClung's initial base salary was $440,000 and her initial target annual bonus opportunity was 40% of her annual base salary. Both of these amounts are subject to review and adjustment by the Compensation Committee from time to time. Additional details about this agreement are provided in *Severance and Change in Control Payments and Benefits* below.

Equity Incentive Plans

2013 Equity Incentive Plan

The 2013 Plan was duly adopted by our Board and approved by our stockholders in November 2013. The 2013 Plan was subsequently amended and the number of shares issuable under the 2013 Plan was increased. The 2013 Plan provided for the grant of incentive stock options ("ISOs"), nonqualified stock options ("NSOs"), stock appreciation rights ("SARs"), restricted stock, and restricted stock units ("RSUs") to our executive officers, directors, employees, and consultants. No further grants have been or will be made under the 2013 Plan after the 2021 Plan (described below) became effective.

The 2013 Plan authorized the issuance of up to 9,954,446 shares of our common stock pursuant to stock options or other awards, plus up to 454,500 shares of our common stock pursuant to stock options or other awards granted under our terminated 2012 Stock Option/Stock Issuance Plan that expired or otherwise terminated without having been exercised in full and shares of our common stock issued pursuant to awards granted under the 2012 Plan that were forfeited to or repurchased by us. As of February 28, 2022, there were outstanding stock options covering 3,810,521 shares granted under the 2013 Plan.

Plan administration. The compensation committee of our Board has the authority to administer the 2013 Plan, including the authority to construe and interpret the 2013 Plan with respect to stock option awards made under the 2013 Plan.

2021 Equity Incentive Plan

The 2021 Plan was duly adopted by our Board in June 2021 and approved by our stockholders in July 2021. The 2021 Plan is a successor to our 2013 Plan. The principal purpose of the 2021 Plan is to attract, retain, and motivate selected employees, directors, and consultants through the granting of stock-based compensation awards. The material terms of the 2021 Plan are summarized below.

Share Reserve. Initially, under the 2021 Plan the maximum number of shares of our common stock that could be issued was 11,232,084 shares, which is the sum of (i) 5,200,000 new shares, plus (ii) an additional number of shares not to exceed 6,032,084, consisting of (A) shares that remained available for issuance of awards under our 2013 Plan immediately prior to the time our 2021 Plan became effective and (B) shares of our common stock subject to outstanding stock options or other awards granted under our 2013 Plan that, on or after the 2021 Plan became effective, terminate or expire prior to exercise thereof, are not issued, are forfeited, or are reacquired or withheld (or not issued) to satisfy a tax withholding obligation or the purchase or exercise price, if any, as such shares become available from time to time. The shares were initially reserved for issuance pursuant to a variety of stock-based compensation awards, including stock options, SARs, restricted stock awards, RSUs, performance stock awards, performance stock unit awards, and other stock-based awards. The number of shares reserved for issuance or transfer pursuant to awards under the 2021 Plan will be increased on the first day of each fiscal year beginning in 2022 and ending in 2031, by an amount equal to the lesser of (i) 5% of the shares of common stock outstanding on the last day of the immediately preceding fiscal year, and (ii) such smaller number of shares of stock as determined by our Board. Pursuant to this provision, 3,013,157 shares of common stock were added to the 2021 Plan reserve on January 1, 2022. No more than 56,000,000 shares of stock may be issued under the 2021 Plan upon the exercise of ISOs. As of February 28, 2022, there were outstanding stock awards covering 2,751,375 shares granted under the 2021 Plan.

The following counting provisions apply to the share reserve under the 2021 Plan:

- to the extent that a stock award terminates, expires, or lapses for any reason or an award is settled in cash without the delivery of shares, any shares subject to the award at such time will be available for future grants under the 2021 Plan;
- to the extent shares are tendered or withheld to satisfy the grant, exercise price, or tax withholding obligation with respect to any award under the 2021 Plan, such tendered or withheld shares will be available for future grants under the 2021 Plan;
- to the extent that shares of our common stock awarded by us are repurchased by us prior to vesting so that shares are returned to us, such shares will be available for future grants under the 2021 Plan;
- the payment of dividend equivalents in cash in conjunction with any outstanding awards will not be counted against the shares available for issuance under the 2021 Plan; and
- to the extent permitted by applicable law or any exchange rule, shares issued in assumption of, or in substitution for, any outstanding awards of any entity acquired in any form of combination by us or any of our subsidiaries will not be counted against the shares available for issuance under the 2021 Plan.

The 2021 Plan includes limits with respect to non-employee directors. A non-employee director shall not receive total compensation for any fiscal year that exceeds $750,000 (or $1,000,000 in the year of the director's initial appointment to our Board). For this purpose, total compensation is the sum of the grant date fair value of any equity or equity-based awards granted to such non-employee director during a fiscal year, and the amount of cash fees or awards payable to such non-employee director in respect of such service during any fiscal year, including any such amounts that are voluntarily deferred by the non-employee director.

Administration. The compensation committee of our Board administers the 2021 Plan with respect to grants to non-officer employees. The compensation committee consists of at least three members of our Board, each of whom is intended to qualify as a "non-employee director" for purposes of Rule 16b-3 under the Exchange Act and an "independent director" within the meaning of the rules of Nasdaq. The 2021 Plan provides that the Board or the compensation committee may delegate its authority to grant awards to employees other than executive officers to our president and chief executive officer.

Subject to the terms and conditions of the 2021 Plan, the administrator has the authority to select the persons to whom awards are to be made, to determine the number of shares to be subject to awards, and the terms and conditions of awards, and to make all other determinations and to take all other actions necessary or advisable for the administration of the 2021 Plan. The administrator is also authorized to adopt, amend, or rescind rules relating to administration of the 2021 Plan. Our Board may at any time remove the compensation committee as the administrator and revest in itself the authority to administer the 2021 Plan. Although the compensation committee of our Board is authorized to administer the 2021 Plan, our Board currently administers the 2021 Plan with respect to awards to non-employee directors and executive officers.

Eligibility. Stock options, SARs, RSUs, restricted stock awards, performance stock, and all other stock-based awards under the 2021 Plan may be granted to individuals who are our employees, directors, or consultants or who are employees, directors, or consultants of certain of our subsidiaries. Only employees of our company or certain of our subsidiaries may be granted ISOs.

Stock Awards. The 2021 Plan provides that the administrator may grant or issue stock options, SARs, restricted stock, RSUs, performance stock, performance stock units, other stock-based awards, and dividend equivalents, or any combination thereof. Each award will be set forth in a separate agreement with the person receiving the award and will indicate the type, terms, and conditions of the award.

- *Nonqualified Stock Options* ("NSOs") will provide for the right to purchase shares of our common stock at a specified price, which may not be less than fair market value on the date of grant. NSOs usually will become exercisable (at the discretion of the administrator) in one or more installments after the grant date, subject to the participant's continued employment or service with us and/or subject to the satisfaction of corporate performance targets and individual performance targets established by the administrator. NSOs may be granted for any term specified by the administrator that does not exceed 10 years.
- *Incentive Stock Options* ("ISOs") will be designed in a manner intended to comply with the provisions of Section 422 of the Internal Revenue Code of 1986, as amended (the "Tax Code") and will be subject to specified restrictions contained in the Tax Code. Among such restrictions, ISOs must have an exercise price of not less than the fair market value of a share of common stock on the date of grant, may only be granted to employees, and must not be exercisable after a period of 10 years measured from the date of grant. In the case of an ISO granted to an individual who owns (or is deemed to own) at least 10% of the total combined voting power of all classes of our capital stock, the 2021 Plan

provides that the exercise price must be at least 110% of the fair market value of a share of common stock on the date of grant and the ISO must not be exercisable after a period of five years measured from the date of grant.

- *Restricted Stock and Performance Stock* may be granted to any eligible individual and made subject to such restrictions as may be determined by the administrator, which in the case of performance stock will include performance-based restrictions. Restricted stock and performance stock, typically, may be forfeited for no consideration or repurchased by us at the original purchase price if the conditions or restrictions on vesting are not met. In general, such stock may not be sold or otherwise transferred until restrictions are removed or expire. Recipients of restricted stock and performance stock, unlike recipients of stock options, have voting rights and have the right to receive dividends, if any, prior to the time when the restrictions lapse; however, extraordinary dividends will generally be placed in escrow, and will not be released until restrictions are removed or expire.

- *Restricted Stock Units and Performance Stock Units* may be awarded to any eligible individual, typically without payment of consideration, but subject to vesting conditions based on continued employment or service or on performance criteria established by the administrator. Like restricted stock and performance stock, these units may not be sold, or otherwise transferred or hypothecated, until vesting conditions are removed or expire. Unlike restricted stock and performance stock, stock underlying these units will not be issued until the units have vested, and recipients of units generally will have no voting or dividend rights prior to the time when vesting conditions are satisfied.

- *Stock Appreciation Rights (*"SARs") may be granted in connection with stock options or other awards, or separately. SARs granted in connection with stock options or other awards typically will provide for payments to the holder based upon increases in the price of our common stock over a set exercise price. The exercise price of any SAR granted under our 2021 Plan must be at least 100% of the fair market value of a share of our common stock on the date of grant. There are no restrictions specified in the 2021 Plan on the exercise of SARs or the amount of gain realizable therefrom, although restrictions may be imposed by the administrator in the SAR agreements. SARs under the 2021 Plan will be settled in cash or shares of our common stock, or in a combination of both, at the election of the administrator.

- *Other Stock-Based Awards* are awards of fully vested shares of our common stock and other awards valued wholly or partially by referring to, or otherwise based on, shares of our common stock. Other stock-based awards may be granted to participants and may also be available as a payment form in the settlement of other awards, as standalone payments, and as payment in lieu of base salary, bonus, fees, or other cash compensation otherwise payable to any individual who is eligible to receive awards. The plan administrator determines the terms and conditions of other stock-based awards, which may include vesting conditions based on continued service, performance, and/or other conditions.

- *Dividend Equivalents* represent the right to receive the equivalent value of dividends paid on shares of our common stock and may be granted alone or in tandem with awards other than stock options or SARs. Dividend equivalents are credited as of dividend payments dates during the period between a specified date and the date such award terminates or expires, as determined by the plan administrator.

Any stock-based award may be granted as a performance award, meaning that the award will be subject to vesting and/or payment based on the attainment of specified performance goals determined by the administrator.

Change in Control. In the event of a change in control where the acquirer does not assume or replace awards granted prior to the consummation of such transaction, awards issued under the 2021 Plan may be subject to accelerated vesting in the discretion of the administrator, such that 100% of such awards will become vested and exercisable or payable, as applicable. In addition, the administrator will also have complete discretion to structure one or more awards under the 2021 Plan to provide that such awards will become vested and exercisable or payable on an accelerated basis in the event such awards are assumed or replaced with equivalent awards, including in such circumstances where the individual's service with us or the acquiring entity is subsequently terminated within a designated period following the change in control event. The administrator may also make appropriate adjustments to awards under the 2021 Plan and is authorized to provide for the acceleration, cash-out, termination, assumption, substitution, or conversion of such awards in the event of a change in control or certain other unusual or nonrecurring events or transactions. Under the 2021 Plan, a change in control is generally defined as:

- the transfer or exchange in a single transaction or series of related transactions by our stockholders of more than 50% of our voting stock to a person or group;

- a change in the composition of our Board such that incumbent directors cease to constitute a majority of our Board;

- the consummation of a merger, consolidation reorganization or business combination, a sale or disposition of all or substantially all of our assets, or the acquisition of assets or stock of another entity, other than a transaction (i) that results in our outstanding voting securities immediately before the transaction continuing to represent a majority of the voting power of the acquiring company's outstanding voting securities; (ii) after which no person or group beneficially owns 50% or more of the outstanding voting securities of the surviving entity immediately after the transaction; and (iii)

after which at least a majority of the board of the successor entities were board members at the time of the approval of the transaction; or

- our liquidation or dissolution.

Adjustments of Awards. In the event of any stock dividend or other distribution, stock split, reverse stock split, reorganization, combination, or exchange of shares, merger, consolidation, split-up, spin-off, recapitalization, repurchase, or any other corporate event affecting the number of outstanding shares of our common stock or the share price of our common stock that would require adjustments to the 2021 Plan or any awards under the 2021 Plan in order to prevent the dilution or enlargement of the potential benefits intended to be made available thereunder, the administrator will make appropriate, proportionate adjustments to:

- the aggregate number and type of shares subject to the 2021 Plan (including the number of shares that may be issued as incentive stock options);
- the number and kind of shares subject to outstanding awards and terms and conditions of outstanding awards (including, without limitation, any applicable performance targets or criteria with respect to such awards); and
- the grant or exercise price per share of any outstanding awards under the 2021 Plan.

Amendment. The administrator may amend or modify the 2021 Plan at any time and from time to time. However, we must generally obtain stockholder approval to the extent required by applicable law, rule, or regulation (including any applicable stock exchange rule). Notwithstanding the foregoing, an option may be amended to reduce the per share exercise price below the per share exercise price of such option on the grant date and options may be granted in exchange for, or in connection with, the cancellation or surrender of options having a higher per share exercise price without receiving additional stockholder approval.

Termination. Our Board may terminate the 2021 Plan at any time. No awards, including incentive stock options, may be granted pursuant to the 2021 Plan after the 10th anniversary of the effective date of the 2021 Plan, and no additional annual share increases to the 2021 Plan's aggregate share limit will occur from and after that anniversary. Any award that is outstanding on the termination date of the 2021 Plan will remain in force according to the terms of the 2021 Plan and the applicable award agreement.

2021 Employee Stock Purchase Plan

Our 2021 ESPP was duly adopted by our Board in June 2021 and approved by our stockholders in July 2021. The principal purpose of the 2021 ESPP is to secure the services of new employees, to retain the services of existing employees, and to provide incentives for such individuals to exert maximum efforts toward our success. The 2021 ESPP includes two components. One component is intended to qualify for favorable tax treatment under Section 423 of the Tax Code. The second component allows for the grant of purchase rights that does not qualify for favorable tax treatment due to deviations in an offering and to permit participation by eligible employees who are employed outside of the United States in compliance with the laws of other jurisdictions.

Shares available. We have initially reserved 511,000 shares of our common stock for sale under the 2021 ESPP. The number of shares reserved for sale under our 2021 ESPP will be increased on the first day of each fiscal year beginning in 2022 and ending in 2031, by an amount equal to the lesser of (i) 1% of the shares of common stock outstanding on the last day of the immediately preceding fiscal year, and (ii) such smaller number of shares of stock as determined by our Board. Pursuant to this provision, 602,631 shares of common stock were added to the 2021 ESPP reserve on January 1, 2022. No more than 10,000,000 shares of our common stock may be issued under the 2021 ESPP over the term of the 2021 ESPP.

Administration. The 2021 ESPP may be administered by the compensation committee of our Board, or by our Board acting in place of our compensation committee, subject to the terms and conditions of the 2021 ESPP. Among other things, the compensation committee has the authority to determine eligibility for participation in the 2021 ESPP, designate separate offerings under the plan, and construe, interpret, and apply the terms of the plan.

Eligibility. Employees eligible to participate in any offering pursuant to the 2021 ESPP generally include any employee who is employed by us or certain of our designated subsidiaries at the beginning of the offering period. However, our compensation committee may determine that employees who are customarily employed for 20 hours or less per week or for five months or less in a calendar year, certain "highly compensated" employees, or employees resident in a foreign jurisdiction whose participation is either prohibited under local law, or where compliance with local law would violate Section 423 of the Tax Code, may not be eligible to participate in the 2021 ESPP. In addition, any employee who owns (or is deemed to own as a result of attribution) 5% or more of the total combined voting power or value of all classes of our capital stock, or the capital stock of one of our qualifying subsidiaries, or who will own such amount as a result of participation in the 2021 ESPP, will not be eligible to participate in the 2021 ESPP. The compensation committee may impose additional restrictions on eligibility from time to time.

Offerings. Under the 2021 ESPP, eligible employees will be offered the option to purchase shares of our common stock at a discount over a series of offering periods. Each offering period may itself consist of one or more purchase periods with purchase dates, and on the purchase dates shares of our common stock will be purchased for employees participating in the offering. No offering period may be longer than 27 months. An offering under the 2021 ESPP may be terminated under certain circumstances.

Participation. Participating employees will be able to purchase the offered shares of our common stock by accumulating funds through payroll deductions or through cash payments. Participants may select a rate of payroll deduction between 1% and 15% of their eligible compensation, as defined in the 2021 ESPP. However, a participant may not subscribe for more than $25,000 in fair market value of shares of our common stock (determined as of the date the offering period commences) in any calendar year in which the offering is in effect.

Unless otherwise determined by the compensation committee, the purchase price for shares of our common stock purchased under the 2021 ESPP will be 85% of the lesser of the fair market value of our common stock on (i) the first trading day of the applicable offering period or (ii) the last trading day of each purchase period in the applicable offering period.

Once an employee becomes a participant in an offering period, the participant will be automatically enrolled in each subsequent offering period at the same contribution level. A participant may reduce their contribution in accordance with procedures set forth by the compensation committee and may withdraw from participation in the 2021 ESPP at any time prior to the end of an offering period, subject to time restrictions specified in the plan or such other time as may be specified by the compensation committee. Upon withdrawal, the accumulated payroll deductions will be returned to the participant without interest.

Adjustments upon Recapitalization. If the number of outstanding shares of our common stock is changed by a stock dividend, recapitalization, stock split, reverse stock split, subdivision, combination, reclassification, or similar change in our capital structure without consideration, then our compensation committee will proportionately adjust the number and class of common stock that is available under the 2021 ESPP, the purchase price and number of shares any participant has elected to purchase, as well as the maximum number of shares that may be purchased by participants. The 2021 ESPP also includes provisions for adjustment in the event a change in corporate structure or similar transaction occurs.

Change in Control. If we experience a corporate transaction, the compensation committee may elect to shorten a purchase period in anticipation of the transaction, in which case the participants' accumulated contributions would be used to purchase shares prior to the consummation of the corporate transactions with the resulting termination of the purchase rights, and/or suspend the plan. Alternatively, it may require outstanding rights to purchase shares to be assumed or an equivalent option substituted by the successor corporation.

Transferability. Participants may not assign, transfer, pledge, or otherwise dispose of payroll deductions or cash payments credited to their account, or any rights with regard to an election to purchase shares pursuant to the 2021 ESPP other than by will or the laws of descent or distribution.

Amendment; Termination. The compensation committee may amend, suspend, or terminate the 2021 ESPP at any time without stockholder consent, except as required by law. The 2021 ESPP will continue until the earlier to occur of (i) termination of the 2021 ESPP by our Board, (ii) issuance of all the shares reserved for issuance under the 2021 ESPP, or (iii) the 10th anniversary of the first purchase date under the 2021 ESPP.

Outstanding Equity Awards at 2021 Fiscal Year-End Table

The following table sets forth information concerning outstanding equity awards held by each of our named executive officers as of December 31, 2021:

	Option awards				
Name	Vesting commencement date	Number of securities underlying unexercised options exercisable (#)	Number of securities underlying unexercised options unexercisable (#)	Option exercise price ($/share)	Option expiration date
Rachel E. Haurwitz, Ph.D.	06/12/2018 (1)	119,310	17,040	2.96	06/11/2023
	03/2/2021 (1)	—	437,201	4.11	03/29/2031
	12/20/2021 (2)	—	411,000	15.16	12/19/2031
Jason V. O'Byrne, M.B.A.	02/08/2021 (1)	—	437,201	4.11	03/29/2031
	06/29/2021 (1)	—	48,966	5.27	06/28/2031
	12/20/2021 (2)	—	147,000	15.16	12/19/2031
Barbara G. McClung, J.D.	06/12/2018 (1)	10	67	2.69	6/11/2028
	10/1/2019 (1)	7,581	67,255	2.69	9/30/2029
	03/2/2021 (1)	—	231,914	4.11	3/29/2031
	12/20/2021 (2)	—	147,000	15.16	12/19/2031

(1) 1/4th of the shares subject to the option vest on the one-year anniversary of the vesting commencement date and an additional 1/48th of the aggregate number of shares subject to the option vest on the corresponding day of each month thereafter (or if there is no such corresponding day, on the last day of the month), subject to continued service by the executive officer through the applicable vesting dates.

(2) 1/48th of the shares subject to the option vest on each monthly anniversary of the vesting commencement date (or if there is no such corresponding day. on the last day of the month), subject to the continued service by the executive officer through the applicable vesting dates.

Severance and Change in Control Payments and Benefits

Officer Employment Agreements with our Named Executive Officers and Other Executive Officers

Our amended and restated officer employment agreements with each of our named executive officers and other executive officers, in some cases their initial employment agreements with us, provide that in the event the executive terminates their employment for "good reason" or we terminate their employment without "cause" (in each case defined in their employment agreements), the executive officers are entitled to receive the following benefits, in addition to any accrued obligations (base salary earned through the date of termination, unpaid expense reimbursements, unused vacation, and vested benefits under any of our employee benefit plans) and subject to their execution of a separation agreement containing a general release of claims in our favor and obligations regarding confidentiality, return of property, and non-disparagement: (i) nine months of base salary (12 months in the case of Dr. Haurwitz); (ii) continuation of healthcare insurance coverage for nine months (12 months in the case of Dr. Haurwitz) or the COBRA health continuation period, whichever ends earlier; and (iii) in the case of Dr. Haurwitz, Mr. O'Byrne, Ms. McClung, and Dr. Kanner, 100% of their unvested stock options as of the effective date of the amended and restated employment agreements, if any, will become immediately vested and immediately prior to the expiration of the three month post-termination exercise period for the stock options, such period will be extended to 12 months for the exercise of stock options (regardless of any language to the contrary in any stock plan then in effect, but subject to the expiration date of the stock options). The amounts payable under items (i) and (ii) will be paid out in substantially equal installments in accordance with our payroll practice over nine months (12 months in the case of Dr. Haurwitz) commencing on the first regularly scheduled payroll date that is at least 30 calendar days after the date of termination, subject to the separation agreement having become fully effective.

In the event that the executive officer's employment is terminated by us without "cause" or the executive officer terminates their employment for "good reason" within 12 months after a change in control, or within three months prior to a change in the ownership or effective control of our company, or in the ownership of a substantial portion of our company's assets under Section 409A of the Tax Code (a "409A Change in Control"), subject to their execution of a separation agreement containing a general release of claims in our favor and obligations regarding confidentiality, return of property, and non-disparagement, the executive officer will be entitled to the benefits set forth above, provided that the number of months of base salary and benefits continuation shall be increased to 12 months (18 months in the case of Dr. Haurwitz) and the executive officer shall be entitled to 1.0 times their target annual bonus (1.5 times in the case of Dr. Haurwitz). The target bonus amount is paid on the first regularly scheduled payroll date that

is at least 30 calendar days after the date of termination (or date of the 409A Change in Control, for an executive officer who is terminated prior to the change in control), and if the change in control is a 409A Change in Control, the severance amounts will be payable as a lump sum on the first regularly scheduled payroll date that is at least 30 calendar days following the termination date (or date of the 409A Change in Control for an executive officer who is terminated prior to the change in control), subject to the separation agreement having become fully effective (for clarity, the COBRA payments set forth above will be paid in accordance with the timing set forth above). In addition, in the event of a termination of employment in the circumstances described in this paragraph, 100% of the executive officer's then unvested stock options and time-based restricted stock will become immediately vested.

Each executive officer's amended and restated employment agreement defines "cause" to mean the occurrence of any one or more of the following, subject to certain notice and cure rights: (i) conduct constituting a material act of misconduct in connection with the performance of their duties, including, without limitation, misappropriation of funds or property of our company; (ii) the commission of any felony or a misdemeanor involving moral turpitude, deceit, dishonesty or fraud, or any conduct that would reasonably be expected to result in material injury or reputational harm to our company if they were retained in their position; (iii) continued non-performance of duties, other than by reason of physical or mental illness, incapacity, or disability, that has continued for more than 30 calendar days following written notice of such non-performance from our Board; (iv) a material violation of our written policies; or (v) failure to cooperate with a bona fide internal investigation or an investigation by regulatory or law enforcement authorities, after being instructed by us to cooperate, or the willful destruction or failure to preserve documents or other materials known to be relevant to such investigation or the inducement of others to fail to cooperate or to produce documents or other materials in connection with such investigation.

Each executive officer's amended and restated employment agreement defines "good reason" to mean the occurrence of any one or more of the following, subject to certain notice and cure rights: (i) a material diminution in their responsibilities, authority, or duties; (ii) the assignment of duties that are materially inconsistent with their position; (iii) a decrease of more than 10% of their base salary except for across-the-board reductions based on our financial performance similarly affecting all of our executive officers; (iv) a change in our company's location at which they perform their duties to a location more than 50 miles driving distance from our original location; and (v) a material breach of the employment agreement by us.

Each executive officer's amended and restated employment agreement defines "change in control" as any of the following: (i) any "person," as such term is used in Sections 13(d) and 14(d) of the Exchange Act, other than us, any of our subsidiaries, or any trustee, fiduciary, or other person or entity holding securities under any employee benefit plan or trust of our company or any of our subsidiaries, together with all "affiliates" and "associates," as such terms are defined in Rule 12b-2 under the Exchange Act, of such person, becomes the "beneficial owner," as such term is defined in Rule 13d-3 under the Exchange Act, directly or indirectly, of securities of our company representing 50% or more of the combined voting power of our then outstanding voting securities, in such case other than as a result of an acquisition of securities directly from our company; or (ii) the date a majority of our Board is replaced during any 12-month period by directors whose appointment or election is not endorsed by a majority of the members of our Board before the date of the appointment or election; or (iii) the consummation of (A) a consolidation or merger of our company where our stockholders, immediately prior to the consolidation or merger, would not, immediately after the consolidation or merger, beneficially own, as such term is defined in Rule 13d-3 under the Exchange Act, directly or indirectly, shares representing in the aggregate more than 50% of the voting shares of our company issuing cash or securities in the consolidation or merger, or of its ultimate parent corporation, if any, or (B) any sale or other transfer, in one transaction or a series of transactions contemplated or arranged by any party as a single plan, of all or substantially all of the assets of our company. Certain of the foregoing events that result solely from an acquisition of securities by us are not considered a "change in control."

Change in Control Provisions Under the 2013 Equity Incentive Plan and the 2021 Equity Incentive Plan

Under the terms of the 2013 Plan, in the event of a merger, consolidation, or other capital reorganization or business combination transaction with or into another corporation, entity or person, or a change in control, each outstanding award will be treated as our Board, or a committee thereof appointed by our Board, determines, including, without limitation, that (i) awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation, or an affiliate thereof, with appropriate adjustments as to the number and kind of shares and prices; (ii) the awards will terminate upon or immediately prior to the consummation of such merger or change in control for no consideration; (iii) outstanding awards will vest and become exercisable, realizable, or payable, or restrictions applicable to an award will lapse, in whole or in part prior to or upon consummation of such merger or change in control, and, to the extent our Board, or a committee thereof appointed by our Board, determines, terminate upon or immediately prior to the effectiveness of such merger or change in control; (iv) the termination of an award or forfeiture of shares that are unvested at the time of the transaction in exchange for an amount of cash and/or property, if any, equal to the excess of the fair market value or the exercise price or purchase price paid or to be paid for the shares subject to the awards; (v) the continuation of such outstanding awards if we are the surviving corporation; or (vi) any combination of the foregoing.

The change in control provisions included in the 2021 Plan are described in *2021 Equity Incentive Plan - Change in Control* above.

Other Elements of Compensation

Retirement Plan

We maintain a defined contribution employee retirement plan, or 401(k) Plan, for our executive officers and employees. Our 401(k) Plan is intended to qualify as a tax-qualified plan under Section 401(a) of the Tax Code. Our 401(k) Plan provides that each participant may contribute up to the lesser of 100% of their compensation or the statutory limit, which was $19,500 for calendar year 2021. Participants who are 50 years or older can also make “catch-up” contributions, which in calendar year 2021 were up to an additional $6,500 above the statutory limit. We currently make matching contributions into the 401(k) Plan on behalf of our participants. We match 100% of eligible contributions up to the first 4% of compensation. Participant contributions are held and invested, pursuant to the participant’s instructions, by the 401(k) Plan trustee.

Employee Benefits

All of our executive officers and employees are eligible to participate in our employee benefit plans, including our medical, dental, vision, and disability and life insurance plans.

No Tax Gross-Ups

We do not make gross-up payments to cover our executive officers’ personal income taxes that may pertain to any of the compensation paid or provided by us.

Limitation of Director and Officer Liability and Indemnification

The Delaware General Corporation Law authorizes corporations to limit or eliminate, subject to specified conditions, the personal liability of directors to corporations and their stockholders for monetary damages for breach of their fiduciary duties. Our amended and restated certificate of incorporation limits the liability of our directors to the fullest extent permitted by Delaware law.

We have director and officer liability insurance to cover liabilities our directors and executive officers may incur in connection with their services to us. Our amended and restated certificate of incorporation and restated bylaws also provide that we will indemnify and advance expenses to any of our directors and executive officers who, by reason of the fact that they are one of our directors or executive officers, is involved in a legal proceeding of any nature. We will repay certain expenses incurred by a director or executive officer in connection with any civil, criminal, administrative, or investigative action or proceeding, including actions by us or in our name. Such indemnifiable expenses include, to the maximum extent permitted by law, attorneys’ fees, judgments, fines, ERISA excise taxes, penalties, settlement amounts, and other expenses reasonably incurred in connection with legal proceedings. A director or executive officer will not receive indemnification if they are found not to have acted in good faith and in a manner they reasonably believed to be in, or not opposed to, our best interest.

We have entered into indemnification agreements with each of our directors and executive officers, as well as our vice president of finance and controller, the form of which is referenced as an exhibit to this Annual Report on Form 10-K. These agreements provide that we will, among other things, indemnify and advance expenses to our directors and executive officers for certain expenses, including attorneys’ fees, judgments, fines and settlement amounts incurred by any such person in any action or proceeding, including any action by us arising out of such person’s services as our director or executive officer, 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 persons as directors and executive officers.

Such limitation of liability and indemnification does not affect the availability of equitable remedies. In addition, we have been advised that in the opinion of the Securities and Exchange Commission, indemnification for liabilities arising under the Securities Act of 1933, as amended (the "Securities Act"), is against public policy as expressed in the Securities Act and is therefore unenforceable.

There is no pending litigation or proceeding involving any of our directors or executive officers in which indemnification will be required or permitted. We are not aware of any threatened litigation or proceeding that may result in a claim for such indemnification.

Non-Employee Director Compensation (2021)

The following table sets forth information concerning the compensation awarded to, earned by or paid to our non-employee directors during 2021. Dr. Haurwitz does not receive compensation for her service as a director. Dr. Haurwitz's compensation as our president and chief executive officer for 2021 and 2020 is included with that of our other named executive officers in the Named Executive Officer Summary Compensation Table above.

Name	Fees Earned or Paid in Cash ($)	Option Awards(1) ($)	Total ($)
Current Directors			
Scott Braunstein, M.D.(2)	$ 28,751	$ 547,553	$ 576,304
Andrew Guggenhime, M.B.A.(3)	$ 49,065	$ 547,168	$ 596,233
Dana Richardson-Heron, M.D.(4)	$ 6,815	$ 591,320	$ 598,135
Natalie Sacks, M.D.(5)	$ 43,082	$ 316,392	$ 359,474
Nancy Whiting, Pharm.D.(6)	$ 18,806	$ 981,183	$ 999,989
Ran Zheng(7)	$ 13,169	$ 813,182	$ 826,351
Former Directors			
Philip Austin(8)	$ —	$ —	$ —
Jeffrey Long-McGie, M.B.A.(9)	$ —	$ —	$ —
Robert Weisskoff, Ph.D.(10)	$ —	$ —	$ —
Santhosh Palani, Ph.D.(11)	$ —	$ —	$ —

(1) The amounts shown represent the grant date fair values of option awards granted in 2021 as computed in accordance with ASC Topic 718. See Note 12 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a discussion of the assumptions used in the calculation of these amounts.
(2) Joined the Board in June 2021
(3) Joined the Board in April 2021
(4) Joined the Board in November 2021
(5) Served on the Board throughout 2021
(6) Joined the Board in August 2021
(7) Joined the Board in September 2021
(8) Resigned from the Board in March 2021
(9) Resigned from the Board in July 2021
(10) Resigned from the Board in March 2021
(11) Resigned from the Board in June 2021

Narrative Disclosure to Non-Employee Director Compensation Table

Director Compensation

Cash Compensation. In fiscal 2021, prior to our initial public offering ("IPO"), our non-employee directors who were not affiliated with a stockholder were each entitled to receive $30,000 per year, paid in arrears in quarterly installments of $7,500. In July 2021, in connection with our IPO, our Board adopted a non-employee director compensation policy under which our non-employee directors are compensated as follows:

- each non-employee director receives an annual cash fee of $40,000;
- any non-executive chair of our Board receives an additional annual cash fee of $35,000;
- each non-employee director who is a member of the audit committee receives an additional annual cash fee of $7,500 ($15,000 for the audit committee chair);
- each non-employee director who is a member of the compensation committee receives an additional annual cash fee of $5,000 ($10,000 for the compensation committee chair); and
- each non-employee director who is a member of the nominating and corporate governance committee receives an additional annual cash fee of $4,000 ($8,000 for the nominating and corporate governance committee chair).

In October 2021, our Board established a science and technology committee and set compensation for that committee as follows:

- each non-employee director who is a member of the science and technology committee receives an additional annual cash fee of $5,000 ($10,000 for the science and technology committee chair).

All cash fees are paid quarterly, in arrears, or upon the earlier resignation or removal of the non-employee director. The amount of each payment is prorated for any portion of a calendar quarter that a non-employee director is not serving on our Board, based on the number of calendar days served by the non-employee director.

Each non-employee director is entitled to reimbursement for reasonable travel and other expenses incurred in connection with attending meetings of our Board and any committee on which they serve.

Equity Compensation. Dr. Braunstein and Mr. Guggenhime each received a stock option grant for 87,440 shares upon joining the Board in June 2021 and April 2021, respectively. Under the compensation policy established following our IPO, non-employee directors are entitled to receive stock option grants for 44,000 shares upon joining the Board. These initial grants vest in three annual installments starting on the first anniversary of the grant date. Non-employee directors are also entitled to receive annual stock option grants for up to 27,500 shares. For the December 2021 annual grants, directors who had been continuously serving on the Board since on or before June 20, 2021 were eligible for options for the full 27,500 shares. Directors who had been continuously serving on the Board starting after June 20, 2021 but on or before September 30, 2021 were eligible for options for 13,750 shares. Dr. Whiting's December 2021 option grant was limited to 13,060 shares in adherence to the limit described in the following paragraph. These annual grants vest as to one-twelfth of the shares each month over a one-year period.

Limit on Non-Employee Director Annual Compensation. Pursuant to our 2021 Plan, there are limits on the annual compensation that may be paid to our non-employee directors. Specifically, a non-employee director may not receive total compensation for any fiscal year that exceeds $750,000 (or $1,000,000 in the year of the director's initial appointment to our Board). For this purpose, total compensation is the sum of the grant date fair value of any equity or equity-based awards granted to a non-employee director during the fiscal year, and the amount of cash fees or awards payable to the non-employee director in respect of their service during any fiscal year, including any amounts that are voluntarily deferred by the non-employee director.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee or nominating and corporate governance committee has currently, or has been at any time, an officer or employee of our company. None of our executive officers currently serves, or has served during the last year, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our Board, compensation committee, or nominating and corporate governance committee.

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

Principal Stockholders

The following table presents information relating to the beneficial ownership of our common stock by the following; ownership is shown as of February 28, 2022 unless otherwise indicated:

- each person, or group of affiliated persons, known by us to own beneficially more than 5% of our outstanding common stock;
- each of our named executive officers and directors; and
- our executive officers and directors as a group.

The number of shares of common stock beneficially owned by each entity, person, executive officer, or director is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares of common stock over which the individual has sole or shared voting power or investment power as well as any shares of common stock that the individual has the right to acquire within 60 calendar days of February 28, 2022, through the exercise of any option, warrant, or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of outstanding common stock is computed on the basis of 60,640,723 shares of our common stock outstanding as of February 28, 2022. We do not have any other class of stock. Shares of common stock that a person has the right to acquire within 60 calendar days of February 28, 2022 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all executive officers and directors as a group. Unless otherwise indicated below, the address for each beneficial owner is c/o Caribou Biosciences, Inc., 2929 7th Street, Suite 105, Berkeley, California 94710.

Name of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
5% or Greater Stockholders:		
PFM Health Sciences, LP and affiliates(1)	4,092,309	6.7%
FMR LLC(2)	3,323,284	5.5%
E.I du Pont de Nemours and Company(3)	3,151,311	5.2%
Named Executive Officers and Directors:		
Rachel E. Haurwitz, Ph.D.(4)	3,632,725	6.0%
Jason V. O'Byrne, M.B.A.(5)	141,657	*
Barbara G. McClung, J.D.(6)	443,898	*
Scott Braunstein, M.D.(7)	45,604	*
Andrew Guggenhime, M.B.A.(8)	52,890	*
Dara Richardson-Heron, M.D	—	—
Natalie R. Sacks, M.D.(9)	87,952	*
Nancy Whiting, Pharm.D.(10)	4,353	*
Ran Zheng(11)	4,583	*
All executive officers and directors as a group (12 persons)(12)	4,864,460	7.9%

* Indicates beneficial ownership of less than 1% of the total issued and outstanding shares of common stock.

(1) As reported on a Schedule 13G/A filed with the SEC on February 14, 2022 by PFM Health Sciences, LP ("PFM"), PFM Health Sciences GP, LLC ("PFM-GP"), PFM Healthcare Growth Equity I, GP, LLC ("HCG-GP"), Partner Asset Management, LLC ("PAM"), and Brian D Grossman ("Grossman") with respect to shares of common stock owned as of December 31, 2021 by PFM Healthcare Master Fund, L.P., a Cayman Islands limited partnership ("HCM"), PFM Healthcare Growth Equity Fund I, LP, a Delaware limited partnership ("HCG"), and Partner Investments, L.P., a Delaware limited partnership ("PI" and, collectively with HCM and HCG, the "Funds"). PFM is the investment advisor for the Funds. HCG-GP is the general partner of HCG. PAM is the general partner of HCM and PI and the member manager of HCG-GP. PFM-GP is the general partner of PFM and the manager of PAM. Grossman is the sole member of PFM-GP. As of December 31, 2021, the beneficial ownership consisted of (i) 4,092,309 shares held by PFM, PFM-GP and PAM with shared voting and dispositive power; (ii) 901,741 shares held by

HCG-GP with shared voting and dispositive power; and (iii) 4,092,309 shares held by Grossman with shared voting and dispositive power. The address of the principal business office for each of PFM, PFM-GP, HCG-GP, PAM, and Grossman is c/o PFM Health Sciences, LP, 475 Sansome Street, Suite 1720, San Francisco, CA 94111.

(2) As reported on a Schedule 13G filed with the SEC on July 29, 2021 by FMR LLC and Abigail P. Johnson (a Director, the Chairman and the Chief Executive Officer of FMR LLC), beneficial ownership as of July 27, 2021consisted of (i) sole voting power of 2,034,156 shares held by FMR LLC, certain of its subsidiaries (including Impresa Management LLC) and affiliates, and other companies and (ii) sole dispositive power of 3,323,284 shares held by each of FMR LLC and Ms. Johnson and certain Johnson family members and trusts. The above entities and certain other entities related to the above entities are subject to a voting limitation that prevents them from voting any shares in excess of 4.99% (in the aggregate) of our total outstanding voting securities on certain matters. The address of FMR LLC is 245 Summer Street, Boston, Massachusetts 02210.

(3) As reported on a Schedule 13G filed with the SEC on March 1, 2022 by E. I. du Pont de Nemours and Company ("DuPont"). The address of the principal business offices for DuPont is 9330 Zionsville Rd., Indianapolis, Indiana 46268.

(4) Consists of (i) 3,349,395 shares of common stock owned by The City Canyon Family Trust dated May 31, 2021, of which Dr. Haurwitz is a co-trust with her spouse, (ii) 10,000 shares of common stock held directly by Dr. Haurwitz, and (iii) 273,330 shares subject to options exercisable within 60 days of February 28, 2022.

(5) Consists of (i) 26,224 shares of common stock owned directly and (ii) 115,433 shares subject to options exercisable within 60 days of February 28, 2022.

(6) Consists of (i) 348,971 shares of common stock owned directly and (ii) 94,927 shares subject to options exercisable within 60 days of February 28, 2022.

(7) Consists of 45,604 shares of common stock subject to options exercisable within 60 days of February 28, 2022.

(8) Consists of 52,890 shares of common stock subject to options exercisable within 60 days of February 28, 2022.

(9) Consists of 87,952 shares of common stock subject to options exercisable within 60 days of February 28, 2022.

(10) Consists of 4,353 shares of common stock subject to options exercisable within 60 days of February 28, 2022.

(11) Consists of 4,583 shares of common stock subject to options exercisable within 60 days of February 28, 2022.

(12) Consists of (i) 3,956,509 shares of common stock held by our executive officers and directorsand (ii) 907,951 shares subject to options exercisable within 60 days of February 28, 2022.

Equity Compensation Plans as of December 31, 2021

The following table shows certain information with respect to all of our equity compensation plans in effect as of December 31, 2021:

Plan Category	Number of securities to be issued upon exercise of outstanding stock options (a)	Weighted-average exercise price of outstanding stock options (b)	Number of securities remaining available for issuance under equity compensation plans (excluding securities reflected in column (a))	
Equity compensation plans approved by stockholders				
2021 Plan(1)	2,402,110	$ 17.59	3,749,300	
2013 Plan	4,355,180	3.59	—	
2021 ESPP(2)	—	—	511,000	(3)
Equity compensation plans not approved by stockholders	—	—	—	
Total	6,757,591	$ 8.57	4,260,300	

(1) The number of shares remaining available for future issuance under the 2021 Plan automatically increases on January 1st each year, through and including January 1, 2031, in an amount equal to the lesser of (i) 5% of the total number of shares of common stock outstanding on such December 31st of the preceding calendar year or (ii) a number of shares as determined by our Board prior to the beginning of each year.

(2) The number of shares remaining available for future issuance under the ESPP automatically increases on January 1st of each year, through and including January 1, 2031, in an amount equal to the lesser of (i) 1% of the total number of shares of common stock outstanding on such December 31st of the preceding calendar year, or (ii) a number of shares as determined by our Board prior to the beginning of each year.

(3) Of these 511,000 shares, 50,781 shares were subject to outstanding purchase rights as of December 31, 2021 and the balance of 460,219 remain available under the 2021 ESPP.

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

Certain Relationships and Related Transactions

The following includes a summary of transactions since January 1, 2021, and any currently proposed transactions, to which we were or are expected to be a participant in which (i) the amount involved exceeded or will exceed $120,000 and (ii) any of our executive officers, directors, or holders of more than 5% of any class of our voting securities, or any affiliate or member of the immediate family of any of the foregoing persons, had or will have a direct or indirect material interest, other than the compensation and other arrangements we describe in the *Executive Compensation* section in Item 11 of this Annual Report on Form 10-K.

Loan to our President and Chief Executive Officer

In November 2018, we entered into a promissory note made by Dr. Haurwitz in favor of us in the principal amount of $1,100,000 with interest at a rate of 3.04% compounded annually, on the unpaid balance of the principal sum. The entire unpaid principal balance of the promissory note, together with the accrued and unpaid interest, would have become due and payable on November 27, 2023. Prepayment of the principal balance of the promissory note, together with accrued and unpaid interest, could have been made in whole or in part at any time without penalty. In order to secure the payment of the promissory note, we entered into a pledge and security agreement with Dr. Haurwitz where she pledged and granted us a security interest in 409,795 shares of our common stock held by her. On June 7, 2021, Dr. Haurwitz repaid the loan in full to us, including approximately $86,573 of accrued interest. Dr. Haurwitz is one of our co-founders, our president and chief executive officer, a director, and a holder of greater than 5% of our common stock.

Amended and Restated Collaboration and License Agreement with Pioneer

In July 2015, we entered into an Amended and Restated Collaboration and License Agreement (as amended, the "Pioneer Agreement") with Pioneer Hi-Bred International, Inc. ("Pioneer"). Pursuant to an amendment in December 2020, to the Pioneer Agreement, Pioneer assigned the chRDNA patent family to us and we agreed to make an upfront payment of $0.5 million; to pay all patent prosecution and maintenance costs going forward; to pay up to $2.8 million in regulatory milestones for therapeutic products developed by us, our affiliates, and licensees; to pay up to $20.0 million in sales milestones over a total of four therapeutics products sold by us, our affiliates, and licensees; and to pay a percentage of sublicensing revenues received by us for licensing the chRDNA patent family. In 2021, we paid Pioneer $0.8 million in sublicensing fees. Pioneer is a wholly-owned subsidiary of DuPont, which holds more than 5% of our common stock. Corteva, Inc. owns 100% of the outstanding common shares of DuPont.

Series C Preferred Stock Financing

In March 2021, PFM Health Sciences, LP and its affiliate funds (together, ("PFM"), and each of Ridgeback Capital Investments LP ("Ridgeback"), and Zone III Healthcare Holdings, LLC, an affiliate of Farallon Capital Management, L.L.C. ("Zone III") purchased 1,158,949 shares of our Series C preferred stock at a purchase price of $17.257 per share, for approximately $20.0 million. Each of PFM, Ridgeback, and Zone III became a beneficial owner of more than 5% of our capital stock as a result of the transaction and remained so until our IPO in July 2021.

AngelList-Cces-Fund, a series of AngelList-JR-Funds, LLC ("AngelList"), was a greater than 5% stockholder of our Series A-1 preferred stock when, in March 2021, we issued an aggregate of 70,122 shares of Series C preferred stock at a purchase price of $17.257 per share, for approximately $1.2 million, to an affiliate of AngelList.

Each of Pacific Continental Investment Company, LLC ("Pacific Continental") and Pontifax Global Food and Agriculture Technology LP ("Pontifax") was a greater than 5% stockholder of our Series B preferred stock when, in March 2021, we issued an aggregate of 135,850 shares of Series C preferred stock at a purchase price of $17.257 per share to Pacific Continental, for approximately $2.3 million, and 135,848 shares of Series C preferred stock at a purchase price of $17.257 per share to Pontifax and two of its affiliates, for approximately $2.3 million.

Participation in our IPO

In our IPO, funds or entities affiliated with PFM, Ridgeback, and Zone III, each of which was one of our greater than 5% stockholders at the time of our IPO, purchased 1,966,500, 187,500, and 1,250,000 shares of our common stock, respectively. Such purchases were made through the underwriters at the IPO price of $16.00 per share for an aggregate purchase price of approximately $54.5 million.

Investors' Rights Agreement

In March 2021, we entered into an amended and restated investors' rights agreement (the "Investors' Rights Agreement"), with each holder of our convertible preferred stock, which included certain holders of more than 5% of a class or series of our capital stock and entities with which certain of our then-directors were affiliated. The Investors' Rights Agreement imposed certain affirmative obligations on us and also granted certain rights to the holders, including certain registration rights with respect to the registrable securities held by them. The Investors' Rights Agreement also provided for a right of first offer in favor of the holders of convertible preferred stock with regard to certain issuances of our capital stock. The Investors' Rights Agreement has terminated in accordance with its terms.

Voting Agreement

In March 2021, we entered into an amended and restated voting agreement (the "Voting Agreement") with certain holders of our common stock and convertible preferred stock, including certain holders of more than 5% of a class or series of our capital stock and entities with which certain of our then-directors were affiliated. The Voting Agreement governed the election or appointment of members of our Board prior to our IPO. Upon the conversion of all outstanding shares of our convertible preferred stock into common stock in connection with the consummation of our IPO, the Voting Agreement terminated.

Right of First Refusal and Co-Sale Agreement

In March 2021, we entered into an amended and restated right of first refusal and co-sale agreement with certain holders of our common stock and convertible preferred stock, including certain holders of more than 5% of a class or series of our capital stock and entities with which certain of our then-directors were affiliated. This agreement provided for rights of first refusal and co-sale relating to the shares of our common stock held by the parties to the agreement. Upon the consummation of our IPO, the amended and restated right of first refusal agreement and co-sale agreement terminated.

Director and Officer Indemnification and Insurance

Our amended and restated certificate of incorporation contains provisions limiting the liability of directors, and our amended and restated bylaws provide that we will indemnify each of our directors and executive officers to the extent not prohibited by the Delaware General Corporation Law or any other applicable law. Our amended and restated certificate of incorporation and amended and restated bylaws also provide us with the authority to indemnify our executive officers, employees, and other individual.

In addition, we have entered into indemnification agreements with each of our directors, executive officers and vice president of finance and controller. We have agreed to indemnify each of them against certain liabilities, costs, and expenses, and have purchased director and officer liability insurance. We also maintain a general liability insurance policy that covers certain liabilities of directors and executive officers arising out of claims based on acts or omissions in their capacities as directors or executive officers. For more information regarding these agreements, see the *Limitations of Director and Officer Liability and Indemnification* section in Part III, Item 11 of this Annual Report on Form 10-K.

Related Person Transaction Policy

In July 2021, our Board of directors adopted a written related person transaction policy setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy covers, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement, or relationship, or any series of similar transactions, arrangements, or relationships, in which we were or are to be a participant, where the amount involved in any fiscal year exceeds $120,000 and a related person had, has, or will have a direct or indirect material interest, including without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness, and employment by us of a related person. In reviewing and approving any such transactions, the audit committee of our Board has primary responsibility to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction.

All of the transactions described in this section occurred prior to the adoption of this policy. However, our Board has historically reviewed and approved any transaction where a director or executive officer had a financial interest, including all of the transactions described above. Prior to approving such a transaction, the material facts as to relationship or interest of the relevant director or executive officer in the agreement or transaction were disclosed to our Board. Our Board took this information into account when evaluating the transaction and in determining whether the transaction was fair to us and in the best interest of all our stockholders.

Director Independence

See the discussion in the *Director Independence* section of Item 10 of this Annual Report on Form 10-K, which is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

Accounting Fees Paid to Deloitte & Touche LLP

The audit committee of our Board has appointed Deloitte & Touch LLP ("Deloitte ") as our independent registered public accounting firm for the fiscal year ending December 31, 2022. Deloitte has served as our independent registered public accounting firm since 2016.

The following table represents aggregate fees billed to us by Deloitte for services related to the fiscal years ended December 31, 2021 and 2020:

	2021	2020
Audit fees(1)	$ 1,450,886	$ 69,000
Audit-related fees(2)	292,500	—
Tax fees(3)	177,335	78,360
All other fees(4)	—	1,895
Total	$ 1,920,721	$ 149,255

(1) Audit fees consist of fees billed for professional services performed by Deloitte for the audit of our annual consolidated financial statements, the review of interim consolidated financial statements, and review of the registration statement on Form S-1 for our IPO, and related services that are normally provided in connection with statutory and regulatory filings or engagements.
(2) Audit related fees consist of fees billed for assurance and related services that are reasonably related to the performance of the audit or review of our consolidated financial statements, such as fees for the adoption of new accounting standards.
(3) Tax fees consist of fees for professional services, including tax consulting, compliance, and transfer pricing services.
(4) All other fees consist of subscription accounting guide paid to Deloitte.

The audit committee has considered whether the provision of non-audit services is compatible with maintaining the independence of Deloitte and has concluded that the provision of such services is compatible with maintaining the independence of Deloitte.

Pre-Approval Policies and Procedures

Pursuant to the charter of the audit committee, the audit committee must pre-approve all audit and permitted non-audit and tax services that may be provided by our independent registered public accounting firm or other independent registered public accounting firms. During 2021 and 2020, services provided by Deloitte were contracted for prior to the formation of the audit committee and were approved by our Board.

The audit committee may also delegate to one or more subcommittees the authority to approve any audit or permitted non-audit and tax services to be provided to us by our independent registered public accounting firm or other registered public accounting firms.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are included in this Annual Report on Form 10-K:

1. The following Report and Consolidated Financial Statements of our company are included in this Annual Report on Form 10-K:

Report of Independent Registered Public Accounting Firm (PCAOB ID No. 34)

Consolidated Balance Sheets

Consolidated Statements of Operations and Comprehensive Loss

Consolidated Statements of Convertible Preferred Stock Stockholders' Equity (Deficit)

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

See Index to Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, incorporated into this item by reference.

2. All financial schedules have been omitted because the required information is either presented in the consolidated financial statements or the notes thereto or is not applicable or required.

3. 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

Exhibit Number	Exhibit Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K, filed with the SEC on July 28, 2021)
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 of the Registrant's Current Report on Form 8-K, filed with the SEC on July 28, 2021)
4.1*	Description of Common Stock
10.1†	Collaboration and License Agreement dated as of February 9, 2021, between the Registrant and AbbVie Manufacturing Management Unlimited Company (incorporated by reference to Exhibit 10.1 of the Form S-1 filed by the Registrant on July 1, 2021 (File No. 333-257604) (the "Form S-1"))
10.2†	Exclusive License Agreement dated as of November 13, 2020, by and between the Registrant and Memorial Sloan Kettering Cancer Center (incorporated by reference to Exhibit 10.2 of the Form S-1)
10.3†	Sale and Assignment Agreement, dated as of January 31, 2020, by and between the Registrant and ProMab Biotechnologies, Inc. (incorporated by reference to Exhibit 10.3 of the Form S-1)
10.4†	Amendment No. 1 to Sale and Assignment Agreement dated as of October 20, 2020, by and between the Registrant and ProMab Biotechnologies, Inc. (incorporated by reference to Exhibit 10.4 of the Form S-1)
10.5†	Amendment No. 2 to Sale and Assignment Agreement dated as of December 15, 2020, by and between the Registrant and ProMab Biotechnologies, Inc. (incorporated by reference to Exhibit 10.5 of the Form S-1)
10.6	Amendment No. 3 to Sale and Assignment Agreement dated May 5, 2020, by and between the Registrant and ProMab Biotechnologies, Inc. (incorporated by reference to Exhibit 10.6 of the Form S-1)
10.7†	Amended and Restated Collaboration and License Agreement, dated as of July 13, 2015, by and between the Registrant and Pioneer Hi-Bred International, Inc. (incorporated by reference to Exhibit 10.7 of the Form S-1)
10.8†	Amendment No. 1 to Amended and Restated Collaboration and License Agreement, dated as of January 21, 2016, by and between the Registrant and Pioneer Hi-Bred International, Inc. (incorporated by reference to Exhibit 10.8 of the Form S-1)
10.9†	Amendment No. 2 to Amended and Restated Collaboration and License Agreement, dated as of July 18, 2016, by and between the Registrant and Pioneer Hi-Bred International, Inc. (incorporated by reference to Exhibit 10.9 of the Form S-1)
10.10†	Amendment No. 3 to Amended and Restated Collaboration and License Agreement, dated as of March 13, 2017, by and between the Registrant and Pioneer Hi-Bred International, Inc. (incorporated by reference to Exhibit 10.10 of the Form S-1)
10.11†	Amendment No. 4 to Amended and Restated Collaboration and License Agreement, dated as of June 26, 2017, by and between the Registrant and Pioneer Hi-Bred International, Inc. (incorporated by reference to Exhibit 10.11 of the Form S-1)
10.12†	Amendment No. 5 to Amended and Restated Collaboration and License Agreement, dated as of May 25, 2018, by and between the Registrant and Pioneer Hi-Bred International, Inc. (incorporated by reference to Exhibit 10.12 of the Form S-1)

10.13†	Amendment No. 6 to Amended and Restated Collaboration and License Agreement, dated as of June 2, 2019, by and between the Registrant and Pioneer Hi-Bred International, Inc. (incorporated by reference to Exhibit 10.13 of the Form S-1)
10.14†	Amendment No. 7 to Amended and Restated Collaboration and License Agreement, dated as of December 18, 2020, by and between the Registrant and Pioneer Hi-Bred International, Inc. (incorporated by reference to Exhibit 10.14 of the Form S-1)
10.15†	Amendment No. 8 to Amended and Restated Collaboration and License Agreement, dated as of December 18, 2020, by and between the Registrant and Pioneer Hi-Bred International, Inc. (incorporated by reference to Exhibit 10.15 of the Form S-1)
10.16†	License Agreement dated as of July 16, 2014, by and between the Registrant and Intellia, LLC (incorporated by reference to Exhibit 10.16 of the Form S-1)
10.17†	Amendment No. 1 to the License Agreement, dated February 2, 2016, by and between the Registrant and Intellia Therapeutics, Inc. as successor in interest to Intellia, LLC (incorporated by reference to Exhibit 10.17 of the Form S-1)
10.18†	Addendum to License Agreement, dated as of February 2, 2016, by and between the Registrant and Intellia Therapeutics, Inc. as successor in interest to Intellia, LLC (incorporated by reference to Exhibit 10.18 of the Form S-1)
10.19†	Leaseback Agreement, dated June 16, 2021, by and between the Registrant and Intellia Therapeutics, Inc. (incorporated by reference to Exhibit 10.19 of Amendment No. 1 to Form S-1 registration statement filed by the Registrant on July 19, 2021 (File No. 333-257604)
10.20†	Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement for a Programmable DNA Restriction Enzyme for Genome Editing, dated December 15, 2016, by and among the Registrant and the other parties thereto (incorporated by reference to Exhibit 10.20 of the Form S-1)
10.21†	Exclusive License Agreement dated as of April 16, 2013, by and among the Registrant, The Regents of the University of California, and the University of Vienna (incorporated by reference to Exhibit 10.21 of the Form S-1)
10.22†	Amendment No. 1 to the Exclusive License Agreement, dated April 16, 2013, by and among the Registrant, The Regents of the University of California, and the University of Vienna (incorporated by reference to Exhibit 10.22 of the Form S-1)
10.23†	Amendment No. 2 to the Exclusive License Agreement, dated April 17, 2013, by and among the Registrant, The Regents of the University of California, and the University of Vienna (incorporated by reference to Exhibit 10.23 of the Form S-1)
10.24†	Amendment No. 3 to the Exclusive License Agreement, dated April 16, 2021, by and among the Registrant, The Regents of the University of California, and the University of Vienna (incorporated by reference to Exhibit 10.24 of the Form S-1)
10.25†	Memorandum of Understanding, dated March 14, 2019, by and among the Registrant, the University of Vienna, and the Regents of the University of California (incorporated by reference to Exhibit 10.25 of the Form S-1)
10.26	Amended and Restated Office/Laboratory Lease, dated March 31, 2021, by and between the Registrant and 2929 Seventh St., LLC (incorporated by reference to Exhibit 10.26 of the Form S-1)
10.27*	First Amendment, dated as of January 11, 2022, to Amended and Restated Office/Laboratory Lease by and between Registrant and 2929 Seventh St., LLC
10.28	Office/Laboratory Lease between the Registrant and 7th Street Property III General Partnership, having a commencement date of January 13, 2022 (incorporated by reference to Exhibit 10.1 of the Form 8-K filed by the Registrant on January 19, 2022)
10.29*	Rider 1 to Office/Laboratory Lease between the Registrant and 7th Street Property III General Partnership, effective as of the lease commencement date of January 13, 2022
10.30+	Officer Employment Agreement by and between the Registrant and Rachel E. Haurwitz, Ph.D., effective as of July 27, 2021 (incorporated by reference to Exhibit 10.1 of the Form 8-K filed by the Registrant on July 28, 2021)
10.31+†*	Compensation Letter, dated February 11, 2022, from the Registrant to Rachel E. Haurwitz, Ph.D.

10.32+	Officer Employment Agreement by and between the Registrant and Jason V. O'Byrne, effective as of July 27, 2021 (incorporated by reference to Exhibit 10.4 of the Form 8-K filed by the Registrant on July 28, 2021)
10.33†*	Offer Letter between the Registrant and Jason V. O'Byrne dated January 5, 2021
10.34+†*	Compensation Letter, dated February 11, 2022, from the Registrant to Jason V. O'Byrne
10.35+	Officer Employment Agreement by and between the Registrant and Barbara G. McClung, J.D., effective as of July 27, 2021 (incorporated by reference to Exhibit 10.3 of the Form 8-K filed by the Registrant on July 28, 2021)
10.36+†*	Compensation Letter, dated February 11, 2022, from the Registrant to Barbara G. McClung, J.D.
10.37+	Officer Employment Agreement by and between the Registrant and Steven B. Kanner, Ph.D., effective as of July 27, 2021 (incorporated by reference to Exhibit 10.2 of the Form 8-K filed by the Registrant on July 28, 2021)
10.38+†*	Compensation Letter, dated February 11, 2022, from the Registrant to Steven B. Kanner, Ph.D.
10.39+*	Officer Employment Agreement by and between the Registrant and Ruhi Khan, effective as of November 8, 2021
10.40+†*	Compensation Letter, dated February 11, 2022, from the Registrant to Ruhi Khan
10.41+†*	Offer Letter, dated October 29, 2021, between the Registrant and Syed Rizvi
10.42+*	Officer Employment Agreement by and between the Registrant and Syed Rizvi, effective as of January 18, 2022
10.43+	2013 Equity Incentive Plan (as originally adopted) (incorporated by reference to Exhibit 99.1 of the Form S-8 filed by the Registrant on July 26, 2021 (the "Form S-8"))
10.44+	2013 Equity Incentive Plan (as amended May 12, 2016) (incorporated by reference to Exhibit 99.2 of the Form S-8)
10.45+	2013 Equity Incentive Plan of the Registrant, as amended and restated April 3, 2019 and as amended March 1, 2021 (incorporated by reference to Exhibit 10.41 of Amendment No. 1 to Form S-1 registration statement filed by the Registrant on July 19, 2021 (File No. 333-257604))
10.46+*	Amendment to 2013 Equity Incentive Plan (effective December 9, 2021)
10.47+	Form of Stock Option Agreement under the 2013 Equity Incentive Plan (as originally adopted and as amended May 12, 2016) (incorporated by reference to Exhibit 99.4 of the Form S-8)
10.48+	Form of Stock Option Agreement under the 2013 Equity Incentive Plan, as amended and restated April 3, 2019 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q for the period ended September 30, 2021 filed by the Registrant on November 11, 2021)
10.49+	2021 Equity Incentive Plan of the Registrant (incorporated by reference to Exhibit 99.6 of the Form S-8)
10.50+*	Form of Employee Stock Option Agreement under the 2021 Equity Incentive Plan of the Registrant
10.51+*	Form of Non-Employee Director Stock Option Agreement under the 2021 Equity Incentive Plan of the Registrant
10.52+*	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2021 Equity Incentive Plan of the Registrant
10.53+	2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 99.7 of the Form S-8)
10.54	Form of Indemnification Agreement between the Registrant and its directors and officers (incorporated by reference to Exhibit 10.50 of the Form S-1)
10.55	Promissory Note, dated November 27, 2018 made by Rachel E. Haurwitz, Ph.D. in favor of the Registrant (incorporated by reference to Exhibit 10.48 of the Form S-1)
10.56	Pledge and Security Agreement, dated November 27, 2018, by and between the Registrant and Rachel E. Haurwitz, Ph.D. (incorporated by reference to Exhibit 10.49 of the Form S-1)
10.57	Series C Preferred Stock Purchase Agreement, dated March 2, 2021, by and among the Registrant and the parties listed therein (incorporated by reference to Exhibit 10.59 of the Form S-1)

10.58	Third Amended and Restated Voting Agreement, dated March 2, 2021, by and among the Registrant and the parties listed therein (incorporated by reference to Exhibit 10.60 of the Form S-1)
10.59	First Amendment to Third Amended and Restated Voting Agreement, dated March 29, 2021, by and among the Registrant and the parties listed therein (incorporated by reference to Exhibit 10.61 of the Form S-1)
10.60	Second Amended and Restated Right of First Refusal and Co-Sale Agreement, dated March 2, 2021, by and among the Registrant and the parties listed therein (incorporated by reference to Exhibit 10.62 of the Form S-1)
10.61	Second Amended and Restated Investors' Rights Agreement, dated March 2, 2021, by and among the Registrant and the investors listed therein (incorporated by reference to Exhibit 4.1 of the Form S-1)
21.1*	List of Subsidiaries of the Registrant
23.1*	Consent of Deloitte & Touche LLP
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Exchange Act, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Exchange Act, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)

* Indicates filed herewith
+ Indicates management contract or compensatory plan
† Indicates certain portions of this document that constitute confidential information have been redacted in accordance with Regulation S-K, Item 601(b)(10)

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Annual Report on Form 10-K (this "Report") to be signed on its behalf by the undersigned, thereunto duly authorized**.**

CARIBOU BIOSCIENCES, INC.

Date: March 21, 2022

By: /s/ Rachel E. Haurwitz
Rachel E. Haurwitz
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Rachel E. Haurwitz **Rachel E. Haurwitz**	President and Chief Executive Officer (Principal Executive Officer); Director	March 21, 2022
/s/ Jason V. O'Byrne **Jason V. O'Byrne**	Chief Financial Officer (Principal Financial Officer)	March 21, 2022
/s/ Ryan Fischesser **Ryan Fischesser**	VP of Finance and Controller (Principal Accounting Officer)	March 21, 2022
/s/ Scott Braunstein **Scott Braunstein**	Director	March 21, 2022
/s/ Andrew Guggenhime **Andrew Guggenhime**	Director	March 21, 2022
/s/ Dara Richardson-Heron **Dara Richardson-Heron**	Director	March 21, 2022
/s/ Natalie R. Sacks **Natalie R. Sacks**	Director	March 21, 2022
/s/ Nancy Whiting **Nancy Whiting**	Director	March 21, 2022
/s/ Ran Zheng **Ran Zheng**	Director	March 21, 2022

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Caribou Biosciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Caribou Biosciences, Inc. and subsidiaries (the "Company") as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

/s/ Deloitte & Touche LLP

San Francisco, California
March 21, 2022

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

CARIBOU BIOSCIENCES, INC. AND ITS SUBSIDIARIES
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	December 31, 2021	December 31, 2020
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 240,420	$ 15,953
Marketable securities, short-term	135,412	—
Accounts receivable	1,153	150
Contract assets ($0 and $250 from related party, respectively)	1,488	1,328
Other receivables	5,483	3,682
Prepaid expenses and other current assets	7,236	3,193
Total current assets	391,192	24,306
NON-CURRENT ASSETS		
Investments in equity securities	7,626	7,626
Marketable securities, long-term	37,676	—
Property and equipment - net	4,887	3,502
Other assets	975	612
TOTAL ASSETS	$ 442,356	$ 36,046
LIABILITIES, CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS' EQUITY (DEFICIT)		
CURRENT LIABILITIES:		
Accounts payable ($0 and $500 to related party, respectively)	$ 3,990	$ 2,601
Accrued expenses and other current liabilities	13,136	8,973
Promissory note — PPP Loan	—	654
Deferred revenue	8,703	161
Total current liabilities	25,829	12,389
LONG-TERM LIABILITIES		
Deferred revenue, net of current portion ($100 and $50 from related party)	22,032	937
Deferred rent and lease incentive liability	2,097	925
Promissory note — PPP Loan, net of current portion	—	924
MSKCC success payments liability	4,080	2,654
Other liabilities	17	176
Deferred tax liabilities	476	155
Total liabilities	54,531	18,160
COMMITMENTS AND CONTINGENCIES (Note 9)		
Convertible preferred stock, par value $0.0001 per share; no shares authorized, issued, and outstanding at December 31, 2021; 7,766,582 shares authorized, issued, and outstanding at December 31, 2020 (liquidation preference $41,620 at December 31, 2020)	—	41,323
STOCKHOLDERS' EQUITY (DEFICIT)		
Preferred stock, par value $0.0001 per share, 10,000,000 and no shares authorized at December 31, 2021 and 2020, respectively; no shares issued and outstanding as of December 31, 2021 and 2020, respectively.	—	—
Common stock, par value $0.0001 per share, 300,000,000 and 28,933,380 shares authorized at December 31, 2021 and 2020, respectively; 60,263,158 and 9,710,829 shares issued and outstanding at December 31, 2021 and 2020, respectively	6	1
Additional paid-in-capital	485,748	7,433
Accumulated other comprehensive loss	(135)	—
Accumulated deficit	(97,794)	(30,871)
Total stockholders' equity (deficit)	387,825	(23,437)
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS' EQUITY (DEFICIT)	$ 442,356	$ 36,046

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

CARIBOU BIOSCIENCES, INC. AND ITS SUBSIDIARIES
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Years Ended December 31,		
	2021	2020	2019
Licensing and collaboration revenue (including $7,250 for the year ended December 2020 from related party, and none for all other periods)	$ 9,598	$ 12,361	$ 5,788
Operating expenses:			
Research and development	52,255	34,425	23,635
General and administrative	24,322	14,060	16,458
Total operating expenses	76,577	48,485	40,093
Loss from operations	(66,979)	(36,124)	(34,305)
Other income (expense):			
Interest income	148	236	1,047
Interest expense	(8)	(20)	(4)
Change in fair value of equity securities	—	(733)	2,294
Change in fair value of the MSKCC success payments liability	(1,426)	—	—
Gain on extinguishment of PPP Loan	1,584	—	—
Other income	79	514	—
Total other income (expense)	377	(3)	3,337
Net loss before provision for (benefit from) income taxes	(66,602)	(36,127)	(30,968)
Provision for (benefit from) income taxes	321	(1,819)	(7,537)
Net loss	(66,923)	(34,308)	(23,431)
Other comprehensive loss:			
Net unrealized loss on available-for-sale marketable securities	(135)	—	—
Net comprehensive loss	$ (67,058)	$ (34,308)	$ (23,431)
Net loss per share, basic and diluted	$ (2.11)	$ (4.01)	$ (2.80)
Weighted-average common shares outstanding, basic and diluted	31,663,243	8,546,741	8,374,674

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

CARIBOU BIOSCIENCES, INC. AND ITS SUBSIDIARIES
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Other Comprehensive Income (Loss)	Retained Earnings (Accumulated Deficit)	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
BALANCE—December 31, 2018	7,766,582	$ 41,323	8,705,171	$ 1	$ 2,574	$ —	$ 27,372	$ 29,947
Retroactive adjustment to beginning retained earnings for adoption of ASC 606	—	—	—	—	—	—	(504)	(504)
Issuance of common stock on exercise of options	—	—	134,033	—	217	—	—	217
Stock-based compensation expense	—	—	—	—	1,234	—	—	1,234
Net loss and comprehensive loss	—	—	—	—	—	—	(23,431)	(23,431)
BALANCE—December 31, 2019	7,766,582	$ 41,323	8,839,204	$ 1	$ 4,025	$ —	$ 3,437	$ 7,463
Issuance of common stock to acquire in-process research and development (Note 4)	—	—	674,196	—	2,136	—	—	2,136
Issuance of common stock on exercise of options	—	—	197,429	—	270	—	—	270
Stock-based compensation expense	—	—	—	—	1,002	—	—	1,002
Net loss and comprehensive loss	—	—	—	—	—	—	(34,308)	(34,308)
BALANCE—December 31, 2020	7,766,582	$ 41,323	9,710,829	$ 1	$ 7,433	$ —	(30,871)	$ (23,437)
Issuance of Series C convertible preferred stock, net of issuance costs of $6.2 million	6,663,940	108,827	—	—	—	—	—	—
Repayment of loan issued by stockholder	—	—	—	—	1,150	—	—	1,150
Conversion of convertible preferred stock into common stock	(14,430,522)	(150,150)	26,234,654	3	150,147	—	—	150,150
Issuance of common stock upon initial public offering, net of issuance costs of $28.6 million	—	—	21,850,000	2	321,018	—	—	321,020
Issuance of common stock on exercise of options	—	—	2,467,675	—	2,551	—	—	2,551
Stock-based compensation expense	—	—	—	—	3,449	—	—	3,449
Net unrealized loss on available-for-sale marketable securities	—	—	—	—	—	(135)	—	(135)
Net loss	—	—	—	—	—	—	(66,923)	(66,923)
BALANCE—December 31, 2021	—	$ —	60,263,158	$ 6	$ 485,748	$ (135)	$ (97,794)	$ 387,825

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

CARIBOU BIOSCIENCES, INC. AND ITS SUBSIDIARIES
Consolidated Statements of Cash Flows
(in thousands)

	Years Ended December 31,		
	2021	2020	2019
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (66,923)	$ (34,308)	$ (23,431)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	984	900	751
Loss on disposal of property and equipment	4	70	1
Change in fair value of equity securities	—	733	(2,294)
Non-cash consideration for licensing and collaboration revenue ($0, $7,500, and $0 from related party, respectively)	—	(7,577)	—
Stock-based compensation expense	3,449	1,002	1,234
Initial fair value of MSKCC success payments liability	—	2,654	—
Change in fair value of MSKCC success payments liability	1,426	—	—
Acquired in-process research and development	1,000	3,134	—
Extinguishment of PPP Loan and accrued interest	(1,578)	—	—
Amortization of premiums on marketable securities	52	—	—
Changes in operating assets and liabilities:			
Accounts receivable	(1,003)	(146)	617
Contract assets	(160)	(492)	(836)
Other receivables	(1,800)	(540)	(870)
Prepaid expenses and other current assets	(4,043)	362	(1,348)
Other assets	(316)	(19)	(298)
Accounts payable	1,139	43	1,176
Accrued expenses and other current liabilities	4,281	2,291	703
Deferred revenue, current and long-term	29,637	(605)	(798)
Deferred rent and lease incentive liability	1,173	25	75
Other liabilities	(162)	(247)	425
Deferred tax liabilities	321	(495)	(7,113)
Net cash used in operating activities	(32,519)	(33,215)	(32,006)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Proceeds from sale of equity securities	—	7,668	28,117
Purchases of property and equipment	(2,121)	(317)	(884)
Proceeds from sale of property and equipment	—	10	—
Payments to acquire in-process research and development	(1,000)	(998)	—
Purchases of marketable securities	(173,276)	—	—
Net cash provided by (used in) investing activities	(176,397)	6,363	27,233
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from initial public offering of common stock, net of offering costs	321,020	—	—
Proceeds from issuance of Series C convertible preferred stock, net of issuance costs	108,827	—	—
Proceeds from exercise of stock options	2,551	270	217
Repayment of promissory note	1,150	—	—
Payments on capital lease	(119)	(113)	(45)
Proceeds from PPP Loan	—	1,578	—
Net cash provided by financing activities	433,429	1,735	172
NET INCREASE (DECREASE) IN CASH, CASH EQUIVALENTS, AND RESTRICTED CASH	224,513	(25,117)	(4,601)
CASH, CASH EQUIVALENTS, AND RESTRICTED CASH — BEGINNING OF PERIOD	15,953	41,070	45,671
CASH, CASH EQUIVALENTS, AND RESTRICTED CASH — END OF PERIOD	$ 240,466	$ 15,953	$ 41,070
RECONCILIATION OF CASH, CASH EQUIVALENTS, AND RESTRICTED CASH			
Cash and cash equivalents	$ 240,420	$ 15,953	$ 41,070
Restricted cash	46	—	—
CASH, CASH EQUIVALENTS, AND RESTRICTED CASH ON THE BALANCE SHEET	$ 240,466	$ 15,953	$ 41,070
SUPPLEMENTAL CASH FLOW INFORMATION:			
Cash paid for income taxes	$ 11	$ 21	$ 1,809
SUPPLEMENTAL SCHEDULE OF NON-CASH INVESTING AND FINANCING ACTIVITIES:			
Purchases of property and equipment unpaid at period end	$ 265	$ 15	$ 886
Capital lease financing for purchase of assets	$ —	$ —	$ 276
Issuance of common stock to acquire in-process research and development (Note 4)	$ —	$ 2,136	$ —
Extinguishment of PPP Loan and accrued interest	$ 1,578	$ —	$ —
Non-cash consideration in exchange for licensing and collaboration revenue	$ —	$ 7,577	$ —
Conversion of convertible preferred stock to common stock at closing of initial public offering	$ 150,150	$ —	$ —

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

1. Description of the Business, Organization, and Liquidity

Business and Organization

Caribou Biosciences, Inc. (the "Company" or "we") is a clinical-stage CRISPR genome-editing biotechnology company. We are developing an internal pipeline of allogeneic chimeric antigen receptor ("CAR") T ("CAR-T") and CAR-natural killer ("CAR-NK") cell therapies. We incorporated in October 2011 as a Delaware corporation and are headquartered in Berkeley, California. We have four wholly-owned subsidiaries: Antler Holdco, LLC, incorporated in Delaware in April 2019; Microbe Holdco, LLC, incorporated in Delaware in June 2020; Arboreal Holdco, LLC, incorporated in Delaware in November 2020; and Biloba Holdco, LLC, incorporated in Delaware in April 2021. Another subsidiary, Caribou Therapeutics Holdco, LLC, was incorporated in Delaware in July 2014 and dissolved in December 2020. Our wholly-owned subsidiaries hold interests in our equity investments and do not have operating activities.

Initial Public Offering

On July 22, 2021, our registration statement on Form S-1 (File No. 333-257604) relating to our initial public offering ("IPO") of common stock became effective. Our IPO closed on July 27, 2021, at which time we issued 19,000,000 shares of our common stock at a price of $16.00 per share. On August 9, 2021, we issued and sold an additional 2,850,000 shares of our common stock to the IPO underwriters pursuant to the full exercise of their over-allotment option to purchase additional shares at the public offering price of $16.00 per share. We received an aggregate of $349.6 million in gross proceeds and approximately $321.0 million in net proceeds from our IPO after deducting underwriting discounts and commissions and offering costs through the issuance of a total of 21,850,000 shares of our common stock. Upon closing of our IPO, all outstanding shares of our convertible preferred stock converted into 26,234,654 shares of our common stock.

In connection with the completion of our IPO, on July 27, 2021, our Certificate of Incorporation was amended and restated to provide for 300,000,000 authorized shares of common stock with a par value of $0.0001 per share and 10,000,000 authorized shares of preferred stock with a par value of $0.0001 per share.

Liquidity

We have incurred net losses and negative cash flows from operations since our inception and we had an accumulated deficit of $97.8 million as of December 31, 2021. During the year ended December 31, 2021, we incurred a net loss of $66.9 million and used $32.5 million of cash in operating activities. We expect to continue to incur substantial losses, and our ability to achieve and sustain profitability will depend on the successful development, approval, and commercialization of our product candidates and on our achievement of sufficient revenue to support our cost structure. We may never achieve profitability and, unless and until we do, we will need to continue to raise additional capital. Our management expects that existing cash, cash equivalents, and marketable securities of $413.5 million as of December 31, 2021, will be sufficient to fund our current operating plan for at least the next 12 months from the date of issuance of our consolidated financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP") and include the accounts of Caribou Biosciences, Inc. and its wholly-owned subsidiaries. All intercompany accounts and transactions are eliminated in consolidation.

Forward Stock Split

In July 2021, our board of directors and stockholders approved an amendment to our certificate of incorporation to effect a forward split of the shares of our outstanding common stock at a ratio of 1.818-for-1 (the "Forward Stock Split"), which became effective July 15, 2021. The number of authorized shares was increased as a result of the Forward Stock Split, but the par values of the common stock and preferred stock were not adjusted. All references to common stock,

options to purchase common stock, common stock share data, per share data, and related information contained in the consolidated financial statements have been retrospectively adjusted to reflect the effect of the Forward Stock Split for all periods presented.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires our management to make estimates and assumptions that affect the reported amounts of assets and liabilities; the disclosure of contingent assets and liabilities at the date of our consolidated financial statements; and the reported amounts of revenue, income, and expenses during the reporting period. On an ongoing basis, we evaluate our estimates and assumptions, including those related to revenue recognition, common stock valuation, stock-based compensation expense, accrued expenses related to research and development activities, valuation of the Memorial Sloan Kettering Cancer Center ("MSKCC") success payments liability, and income taxes. Our management bases its estimates on historical experience and on various other assumptions that they believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from those estimates.

Segments

We operate and manage our business as one reportable and operating segment, which is the business of developing an internal pipeline of allogeneic CAR-T and CAR-NK cell therapies. Our president and chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for allocating resources and evaluating financial performance. All long-lived assets are maintained in the United States.

Concentrations of Credit Risk and Other Uncertainties

Financial instruments that potentially subject us to concentration of credit risk consist of cash and cash equivalents, accounts receivable, contract assets, other receivables, and investments in marketable securities and equity securities. Substantially all of our cash and cash equivalents are deposited in accounts at two financial institutions, and account balances may at times exceed federally insured limits. We also mitigate the risks by investing in high-grade instruments, limiting our exposure to one issuer, and we monitor the ongoing creditworthiness of the financial institutions and issuers. We believe the financial institutions to be of high credit quality.

Licensees that represent 10% or more of our revenue and accounts receivable and contract assets are as follows:

	Revenue			Accounts Receivable and Contract Assets	
	Years Ended			As of December 31,	
	December 31, 2021	December 31, 2020	December 31, 2019	2021	2020
Licensee A	*	*	38.9%	*	*
Licensee B	22.7%	14.5%	26.1%	24.6%	40.6%
Licensee C	*	*	10.6%	*	*
Licensee D, related party	*	60.7%	*	*	*
Licensee E	41.4%	*	*	45.1%	*
Licensee F	*	*	*	*	13.2%
Licensee G, related party	*	*	*	*	16.9%
Licensee H	*	*	*	*	10.1%
Licensee I	*	*	*	*	*
Total	64.1%	75.2%	75.6%	69.7%	80.8%

*Less than 10%

We monitor economic conditions to identify facts or circumstances that may indicate if any of our accounts receivable are not collectible or if the contract assets should be impaired. No allowance for doubtful accounts was recorded as of December 31, 2021 and 2020, respectively.

Revenue Recognition

We determine whether agreements are within the scope of Accounting Standard Codification ("ASC") Topic 606, Revenue from contracts with customers, ("ASC 606") or other topics at the effective date of an agreement. For agreements that are determined

to be within the scope of ASC 606, revenue is recognized when a licensee, or customer, obtains control of promised goods or services (e.g., an intellectual property license). The amount of revenue recognized reflects the consideration that we expect to be entitled to receive in exchange for these goods and services. To achieve this core principle, we apply the following five steps (i) identify the contract with the customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when or as we satisfy a performance obligation.

Our revenues are primarily derived through license and/or license and collaboration agreements. The terms of these types of agreements may include (i) licenses for our technology, (ii) research and development services, and (iii) services or obligations in connection with our participation in research or governance committees. Payments to us under these arrangements typically include one or more of the following: nonrefundable upfront license fees, maintenance fees, milestones, and other contingent payments to us for the achievement of defined collaboration objectives and certain preclinical, clinical, regulatory, and sales-based events, as well as royalties on sales of any commercialized products.

We assess whether the promises in our arrangements with customers are considered distinct performance obligations that should be accounted for separately. Judgment is required to determine whether a license to our intellectual property is distinct from research and development services or participation on research or governance committees.

If a license to intellectual property controlled by us is determined to be distinct from the other performance obligations identified in the agreement, we recognize revenues allocated to the license at the point in time when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are combined with other promises, we utilize our judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress using the input method for each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Certain of our license agreements as well as our license and collaboration agreement include contingent milestone payments. Such milestone payments are typically payable when the collaborator or licensee achieves certain predetermined clinical, regulatory, and/or commercial milestones. Milestone payments that are not within our control or the control of the collaborator or licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At each reporting date, we reevaluate whether the milestones are considered probable of being reached, and we estimate the amount to be included in the transaction price by using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price in such period of determination.

Our license and or collaboration and license agreements may also include contingent payments related to sales-based milestones. Sales-based milestones are typically payable when annual sales of a covered product reach specified levels. Sales-based milestones are recognized at the later of when the associated performance obligation has been satisfied or when the sales occur. Unlike other contingency payments, such as regulatory milestones, sales-based milestones are not included in the transaction price based on estimates at the inception of the contract, but rather, are included when the sales or usage occur. We use the sales-based royalty exception because the license is a predominant item to which sales-based royalties relate.

Certain of our license agreements have two performance obligations: a license and a material right for annual license renewals. Such license agreements require payments of non-refundable annual license fees by the licensee (referred to as maintenance fees in the license agreements), which are accounted for as material rights for license renewals. We recognize revenue when the license is delivered and the term commences. Revenue for the material right for license renewals is recognized at the point in time that the annual license fee is paid by the licensee and the renewal period begins.

Customer payments are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until we satisfy our performance obligations under these arrangements. Amounts payable to us are recorded as accounts receivable if invoiced or as contract assets, when our right to consideration is unconditional.

Fair Value Measurements

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability (Note 3).

Cash and Cash Equivalents

We consider all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents. As of December 31, 2021, cash and cash equivalents consisted of cash, money market funds, and commercial paper securities. As of December 31, 2020, cash and cash equivalents consisted of cash and money market funds.

Restricted Cash

We define restricted cash as cash and cash equivalents that cannot be withdrawn or used for general operating activities. Our restricted cash consists of a letter of credit with a financial institution related to one of our workers' compensation insurance policies. As of December 31, 2021, we had less than $0.1 million of restricted cash, which was recorded in other assets in our consolidated balance sheets. We did not have any restricted cash as of December 31, 2020.

Marketable Securities

Our short-term and long-term marketable securities are available for sale securities and consist of U.S. Treasury bills, commercial paper, U.S. government agency bonds, and corporate debt securities. We classify those securities that mature in more than 12 months as long-term investments in the consolidated balance sheets. We record at estimated fair value based on quoted market prices or observable market inputs of almost identical assets, with the unrealized holding gains or losses recorded in other comprehensive loss in the consolidated statements of operations and comprehensive loss. The amortized cost of securities is adjusted for amortization of premiums and accretion of discounts to maturity, which are both recorded to interest income in the consolidated statements of operations and comprehensive loss.

Changes in the fair value of available-for-sale securities impact the consolidated statements of operations and comprehensive loss only when such securities are sold, or if an impairment is recognized. Realized gains and losses on the sale of securities are determined by specific identification of each security's cost basis. We regularly review our investment portfolio to determine if any security is impaired, which would require us to record an impairment charge in the period any such determination is made. In making this judgment, we consult with our investment managers and consider available quantitative and qualitative evidence in evaluating potential impairment of our investments on a quarterly basis. If the cost of an individual investment exceeds its fair value, we evaluate, among other factors, general market conditions, the duration and extent to which the fair value is less than cost, and our intent and ability to hold the investment. Once a decline in fair value is determined to be other-than-temporary, an impairment charge will be recorded to other expense, net, in the consolidated statements of operations and comprehensive loss and a new cost basis in the short-term investment will be established. During the year ended December 31, 2021, we did not record any impairment related to other-than-temporary declines in the fair value of our marketable securities. We did not have any short-term and long-term marketable securities as of December 31, 2020.

Investments in Equity Securities

We may receive as consideration under our license agreements equity securities of private or public companies (an "investee"). If we determine that we do have control over these investees under either the Variable Interest Entity ("VIE") or voting models, we then determine if we have an ability to exercise significant influence via voting interests, board of director representation, or other business relationships. If we conclude that we do not have an ability to exercise significant influence over an investee, we account for our investment at fair value and may elect to account for an equity security without a readily determinable fair value using a measurement alternative. This measurement alternative allows us to measure the equity investment at its cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer.

During the year ended December 31, 2020, we sold our remaining common stock in Intellia Therapeutics, Inc. ("Intellia") for $7.7 million of cash proceeds. Intellia shares are publicly traded and were accounted for at fair value, which was Intellia's closing price of common stock on Nasdaq at the end of each reporting period. We recognized changes in fair value of $0.7 million in other income (expense) in the consolidated statements of operations and comprehensive loss until the Intellia shares were sold.

As of December 31, 2021 and 2020, investments in equity securities, long-term, consisted primarily of our investment in the preferred stock of a private company, related party (Note 7). We concluded that our shares of the private company's preferred stock are not in substance common stock and, since these securities do not have readily determinable fair value, we account for our investment in the private company's preferred stock using the alternative measurement method. As of December 31, 2021 and 2020, we did not recognize any impairment loss related to this investment.

Property and Equipment

Property and equipment are recorded at cost, net of accumulated depreciation. Depreciation is recorded using the straight-line method over the estimated useful lives of the assets, generally three to 10 years. Leasehold improvements are capitalized and amortized over the shorter period, expected life or lease term. Major replacements and improvements are capitalized, while general repairs and maintenance are expensed as incurred.

Upon retirement or sale of the assets, the cost and related accumulated depreciation and amortization are removed from the consolidated balance sheets and the resulting gain or loss are recorded in the consolidated statements of operations and comprehensive loss.

Impairment of Long-Lived Assets

We evaluate the carrying amount of our long-lived assets whenever events or changes in circumstances indicate that the assets may not be recoverable. An impairment loss is recognized when estimated future cash flows expected to result from the use of the asset and its eventual disposition is less than the carrying amount of the asset. To date, there have been no such impairment losses.

Leases

Our lease agreements for our laboratory and office facilities are classified as operating leases. Rent expense is recognized on a straight-line basis over the term of the lease. Incentives granted under our facilities leases, including allowances to fund leasehold improvements and rent holidays, are recorded to a deferred rent and lease incentive liability and are recognized as reductions to rental expense on a straight-line basis over the term of the leases.

Lease agreements that contain a bargain purchase option, a full transfer of ownership at the completion of the lease term, a lease term that is at least 75% of the useful lives of the assets, or present value of payments in excess of 90% of fair market value of the leased asset are accounted for as capital leases. We capitalize capital leases in property and equipment and the related amortization of assets under capital leases is included in depreciation and amortization expense in our consolidated statements of operations and comprehensive loss. Initial asset values and lease obligations are based on the present value of future minimum lease payments.

Deferred Issuance Costs

Issuance costs, consisting of legal, accounting, audit, and filing fees relating to in-process equity financings, including our IPO, are capitalized. Deferred issuance costs are offset against offering proceeds upon the completion of an equity financing or an offering. In the event an equity financing or an offering is terminated or delayed, deferred issuance costs will be expensed immediately as a charge to general and administrative expenses in the consolidated statements of operations and comprehensive loss. As of December 31, 2021 and 2020, we did not capitalize any issuance costs.

Convertible Preferred Stock

We recorded convertible preferred stock at fair value on the dates of issuance, net of issuance costs. The convertible preferred stock was recorded outside of stockholders' equity (deficit) because the preferred shares contain liquidation features outside of our control. We elected not to adjust the carrying values of the convertible preferred stock to the liquidation preferences of such shares because it is uncertain whether or when an event would occur that would obligate us to pay the liquidation preferences to holders of shares of convertible preferred stock. All outstanding convertible preferred stock converted into common stock in connection with the closing of our IPO and were reclassified to common stock and additional paid-in-capital.

MSKCC Success Payments Liability

Under the terms of our Exclusive License Agreement, dated November 13, 2020, with MSKCC (Note 4), we are obligated to make success payments and a change of control payment if our stock price increases by certain multiples of increasing value based on a comparison of the fair market value of our common stock with $5.1914 per share, adjusted for any future stock splits, during a specified time period. The success payments liability is accounted for under ASC 815, Derivatives and Hedging. The nature of the success payments liability is contingent consideration for the MSKCC exclusive license and, as such, it was accounted for as research and development expenses at estimated fair value at inception. The success payments liability is remeasured at fair value at each subsequent balance sheet date, and changes in the fair value of the success payments liability are included in other income (expense) in the consolidated statements of operations and comprehensive loss.

To determine the estimated fair value of the MSKCC success payments liability, we use a Monte Carlo simulation methodology that models the future movement of stock prices based on several key variables. The following variables were incorporated in the estimated fair value of the success payments liability: estimated term of the success payments, fair value of common stock, expected volatility, risk-free interest rate, and estimated number and timing of valuation measurement dates on the basis of which payments may be triggered. The computation of expected volatility was estimated using a combination of available information about the historical volatility of stocks of similar publicly traded companies for a period matching the expected term assumption and projected volatility. There are several valuation measurement dates that may trigger payments under the MSKCC Agreement and are considered in our valuation of the MSKCC success payments liability (Note 4).

Research and Development Expenses and Accrued Liabilities

Research and development expenses are charged to expense as incurred. Research and development expenses include certain payroll and personnel expenses; laboratory supplies; consulting costs; external clinical research and development expenses; and allocated overhead, including rent, equipment depreciation, and utilities.

We record accrued liabilities for estimated costs of our research and development activities conducted by third-party service providers. We record the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced and include these costs in accrued liabilities in the consolidated balance sheets and within research and development expenses in the consolidated statements of operations and comprehensive loss. We accrue for these costs based on factors such as estimates of the work completed and in accordance with the third-party service agreements. If we do not identify costs that have begun to be incurred or if we underestimate or overestimate the level of services performed or the costs of these services, actual expenses could differ from our estimates. To date, we have not experienced any material differences between accrued costs and actual costs incurred.

We make payments in connection with clinical trials to contract manufacturing organizations (“CMOs”) that manufacture the material for our product candidates and to clinical research organizations (“CROs”) and clinical trial sites that conduct and manage our clinical trials. The financial terms of these contracts are subject to negotiation, which vary by contract and may result in payments that do not match the periods over which materials or services are provided. Generally, these agreements set forth the scope of work to be performed at a fixed fee, unit price or on a time and materials basis. In the event we make advance payments for goods or services that will be used or rendered for future research and development activities, the payments are deferred and capitalized as a prepaid expense and recognized as expense as the goods are received or the related services are rendered. These payments are evaluated for current or long-term classification based on when they are expected to be realized.

Acquisition of In-Process Research and Development Assets

We measure and recognize acquired in-process research and development assets, which include licenses, know-how, patents, and transaction fees, at cost. Goodwill is not recognized in asset acquisitions. If acquired in-process technology is determined to not have an alternative future use, the cost is charged to research and development expenses at the acquisition date.

Patent Costs

We expense costs as incurred for filing, prosecuting, and maintaining patents and patent applications, including certain of the patents and patent applications that we license from third parties. We classify these costs as general and administrative expenses in our consolidated statements of operations and comprehensive loss. In addition, we are entitled to receive reimbursement from third parties for a portion of the filing, prosecution, and maintenance costs for certain patents and patent applications. We accrue for these reimbursements as the respective expenses are incurred, and we classify such reimbursements as a reduction of general and administrative expenses. During the years ended December 30, 2021, 2020, and 2019, we incurred gross patent costs of $12.3 million, $11.2 million, and $8.5 million, respectively. During the years ended December 31, 2021, 2020, and 2019, we recorded $7.1 million, $5.8 million, and $4.4 million, respectively, of patent cost reimbursements as a credit to general and administrative expenses.

Stock-Based Compensation Expense

Stock-based compensation expense related to awards to employees is measured at the grant date based on the fair value of the award. The fair value of the award that is ultimately expected to vest is recognized as expense on a straight-line basis over the requisite service period of the awards, which is generally the vesting period, and is adjusted for pre-vesting forfeitures in the period in which the forfeitures occur.

We use the Black-Scholes valuation model as the method for determining the estimated fair value of stock options and stock purchases under our 2021 Employee Stock Purchase Plan ("ESPP") with the following assumptions:

Fair Market Value of Common Stock — Prior to our IPO, the fair market value of our common stock was determined by our board of directors with assistance from management and external valuation experts. Our approach to estimating the fair market value of our common stock was consistent with the methods outlined in the American Institute of Certified Public Accountants' Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Following our IPO, the fair market value of our common stock is based on its closing price on Nasdaq as reported on the date of the stock option grant.

Expected Term — Expected term represents the period that our stock-based awards are expected to be outstanding and is determined using the simplified method. The expected term for our stock purchases under our ESPP is the offering period.

Expected Volatility — Expected volatility is estimated based on the average historical volatilities of common stock of comparable publicly traded entities over a period equal to the expected term of the stock option grants, as we do not have sufficient trading history for our common stock. Comparable companies are chosen based on their size, stage in the life cycle, or area of specialty. We will continue to apply this process for stock options and ESPP stock purchases until enough historical information regarding the volatility of our stock price becomes available.

Expected Dividends — Expected dividends is zero as we have never paid dividends on our common stock and have no plans to do so for the foreseeable future.

Risk-Free Interest Rate — Risk-free interest rate is based on the U.S. Treasury zero-coupon issued in effect at the time of grant for periods corresponding with the expected term of the award.

Stock-based compensation expense related to awards to non-employees, such as consultants, is recognized based on the then-current fair value at each grant date over the associated service period of the award, which is generally the vesting term, using the straight-line method. The fair value of non-employee stock options and restricted stock awards is estimated using the Black-Scholes valuation model with assumptions generally consistent with those used for employee stock options.

Income Taxes

We account for income taxes using the asset and liability method. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the consolidated financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax.

Other Income

We recognize fees earned from sources not considered to be within the normal course of business in other income within the statements of operations and comprehensive loss. During the year ended December 31, 2021, we recognized $0.1 million of other income mainly related to receiving corporate credit card rewards. During the year ended December 31, 2020, we recognized $0.5 million related to the sale of certain patents and patent applications, which was not an ordinary business activity.

Comprehensive Loss

Comprehensive loss is composed of net loss and other comprehensive income (loss). Other comprehensive income (loss) consists primarily of unrealized gains and losses on available-for-sale marketable securities.

Net Loss Per Share

Basic net loss per share is computed by dividing the net loss by the weighted-average number of common shares outstanding during the period, without consideration of potential dilutive securities. Diluted net loss per share is computed by dividing the net loss by the sum of the weighted-average number of common shares outstanding during the period plus the dilutive effects of potentially dilutive securities outstanding during the period. Potentially dilutive securities include convertible preferred shares, common stock

options, and common shares subject to nonrecourse notes. For all periods presented, diluted net loss per share is the same as basic net loss per share since the effect of including potential common shares is anti-dilutive.

Prior to the conversion of our preferred stock in connection with our IPO, we used the two-class method to calculate net loss per share. Our convertible preferred stock contained participation rights in any dividend paid by us and was deemed to be a participating security. Participating securities did not have a contractual obligation to share in losses. As such, the net loss was attributed entirely to common stockholders.

For all periods presented, diluted net loss per share is the same as basic net loss per share since the effect of including potential common shares is anti-dilutive.

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board (the "FASB") or other standard-setting bodies and adopted by us as of the specified effective date.

New Accounting Pronouncements Not Yet Adopted

In February 2016, the FASB issued Accounting Standards Update ("ASU") No. 2016-02, Leases (Topic 842). This ASU requires a lessee to recognize in its statement of financial position a liability to make lease payments (the lease liability) and a right-to-use asset representing its right to use the underlying asset for the lease term. We may elect not to apply Topic 842 to short-term leases with a term of 12 months or less. We will adopt the new standard as of January 1, 2022, using the modified retrospective method and record a cumulative catch-up to our accumulated deficit. We also plan to elect the package of practical expedients permitted under the transition guidance, which allows us to carry forward the historical lease classification of contracts entered into prior to January 1, 2022. We identified our lease portfolio and are in the process of calculating the impact of this standard. We are also implementing new processes and controls to account for leases in accordance with the new standard. We believe the most significant changes to our consolidated financial statements will relate to the recognition of right-of-use assets and offsetting lease liabilities for operating leases in our consolidated balance sheets. We do not expect the standard to have a material impact on our cash flows or results of operations.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments—Credit Losses: Measurement of Credit Losses on Financial Instruments (Topic 326). This ASU provides guidance on the measurement of credit losses for most financial assets and certain other instruments that are not measured at fair value through net income. ASU 2016-13 will replace the current incurred loss impairment approach with a methodology to reflect expected credit losses and it requires consideration of a broader range of reasonable and supportable information to explain credit loss estimates. This ASU is to be applied on a modified retrospective approach and is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2022, and interim reporting periods within fiscal years beginning after December 15, 2023. Early adoption is permitted. We do not expect that the adoption of this ASU will have a significant impact on our consolidated financial statements.

Emerging Growth Company

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

We may early adopt multiple accounting standards, as the JOBS Act does not preclude an emerging growth company from adopting a new or revised accounting standard earlier than the time that such standard applies to private companies to the extent early adoption is allowed by the accounting standard. We expect to use the extended transition period for any other new or revised accounting standards during the period in which we remain an emerging growth company.

3. Fair Value Measurements of Financial Instruments

The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Quoted prices in active markets for identical assets or liabilities.

Level 2—Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Assets and liabilities measured at fair value are classified in their entireties based on the lowest level of input that is significant to the fair value measurement. Our assessment of the significance of a particular input to the fair value measurement in its entirety requires our management to make judgments and consider factors specific to the asset or liability.

Our financial instruments consist of Level 1, Level 2, and Level 3 financial instruments. We generally classify our marketable securities as Level 2. Instruments are classified as Level 2 when observable market prices for identical securities that are traded in less active markets are used. When observable market prices for identical securities are not available, such instruments are priced using benchmark curves, benchmarking of like securities, sector groupings, matrix pricing, and valuation models. These valuation models are proprietary to the pricing providers or brokers and incorporate a number of inputs, including in approximate order of priority: benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers, and reference data including market research publications. For certain security types, additional inputs may be used, or some of the standard inputs may not be applicable. Evaluators may prioritize inputs differently on any given day for any security based on market conditions, and not all inputs listed are available for use in the evaluation process for each security evaluation on any given day. Level 1 financial instruments are comprised of money market funds and U.S. Treasury bills. Financial assets and liabilities are considered Level 3 when their fair values are determined using pricing models, discounted cash flow methodologies, or similar techniques, and at least one significant model assumption or input is unobservable. Level 3 financial instruments consist of the MSKCC success payments liability.

The following table sets forth our financial instruments that were measured at fair value on a recurring basis by level within the fair value hierarchy (in thousands):

	Fair Value Measurements as of December 31, 2021			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market fund investments (included in cash and cash equivalents)	$ 181,528	$ 181,528	$ —	$ —
Commercial paper ($58,892 included in cash and cash equivalents)	141,676	—	141,676	—
Corporate debt securities	38,649	—	38,649	—
U.S. Treasury bills	26,590	26,590	—	—
U.S. government agency bonds	25,065	—	25,065	—
Total fair value of assets	$ 413,508	$ 208,118	$ 205,390	$ —
Liabilities:				
MSKCC success payments liability	$ 4,080	$ —	$ —	$ 4,080
Total fair value of liabilities	$ 4,080	$ —	$ —	$ 4,080

	Fair Value Measurements as of December 31, 2020			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market fund investments (included in cash and cash equivalents)	$ 15,953	$ 15,953	$ —	$ —
Total fair value of assets	$ 15,953	$ 15,953	$ -	$ —
Liabilities:				
MSKCC success payments liability	$ 2,654	$ —	$ —	$ 2,654
Total fair value of liabilities	$ 2,654	$ —	$ —	$ 2,654

The fair value and amortized cost of cash equivalents and available-for-sale marketable securities by major security type as of December 31, 2021 are presented in the following table (in thousands):

	As of December 31, 2021			
	Amortized Cost Basis	Unrealized Gains	Unrealized Losses	Estimated Fair Value
Money market investments (included in cash equivalents)	$ 181,528	$ -	$ —	$ 181,528
Commercial paper ($58,892 included in cash equivalents)	141,726	1	(51)	141,676
U.S. government agency bonds	25,102	-	(37)	25,065
Corporate debt securities	38,661	4	(16)	38,649
U.S. Treasury bills	26,626	1	(37)	26,590
Total cash equivalents and marketable securities	$ 413,643	$ 6	$ (141)	$ 413,508
Classified as:				
Cash equivalents				$ 240,420
Marketable securities, short-term				135,412
Marketable securities, long-term				37,676
Total cash equivalents and marketable securities				$ 413,508

As of December 31, 2021, our available-for-sale marketable securities had been in a continuous unrealized loss position, each for less than 12 months. As of December 31, 2021, no significant facts or circumstances were present to indicate a deterioration in the creditworthiness of the issuers of the available-for-sale marketable securities we hold, and we have no requirement or intention to sell these securities before maturity or recovery of their amortized cost basis. We considered the current and expected future economic and market conditions surrounding the COVID-19 pandemic and determined that our investments were not significantly impacted. For each security with a fair value less than its amortized cost basis, we determined the decline in fair value below amortized cost basis to be immaterial, and therefore no other than temporary impairment loss has been recorded. During the years ended December 31, 2021, 2020, and 2019, we did not recognize any impairment losses on our investments.

The following table sets forth a summary of the changes in the fair value of our Level 3 financial liability (in thousands):

	MSKCC Success Payments Liability
Balance at January 1, 2020	$ —
Fair value at issuance	2,654
Change in fair value	—
Balance at December 31, 2020	$ 2,654
Change in fair value	1,426
Balance at December 31, 2021	$ 4,080

Our liability for the MSKCC success payments is carried at fair value and changes are recognized as expense or income as part of other income (expense) until the success payments liability is paid or expires (Note 4). The fair value of the MSKCC success payments liability at the issuance date, November 13, 2020 (the effective date of the MSKCC Agreement), was $2.7 million and the change in fair value from the issuance date to December 31, 2020 was not material to our consolidated financial statements. We

recorded $1.4 million change in fair value of the MSKCC success payments liability in other income (expense) in our consolidated statements of operations and comprehensive loss for year ended December 31, 2021.

We utilize a Monte Carlo simulation model that models the future movement of stock prices based on several key variables. This model requires significant estimates and assumptions in determining the estimated fair value of the MSKCC success payments liability at each balance sheet date. The assumptions used to calculate the fair value of the MSKCC success payments are subject to a significant amount of judgment including the expected volatility that was estimated using available information about the historical volatility of stocks of publicly traded companies that are similar to us, the estimated term, and the estimated number and timing of valuation measurement dates. The table below summarizes key assumptions used in the valuation of MSKCC success payments liability:

	As of December 31, 2021	As of December 31, 2020
Fair value of common stock	$ 15.09	$ 5.46
Risk-free interest rate	1.52%	0.93%
Expected volatility	75%	80%
Probability	7.0% to 20.9%	4.4% to 13.4%
Expected term (years)	4.2 to 5.5	4.7 to 5.7

The computation of expected volatility was estimated using a combination of available information about the historical volatility of stocks of similar publicly traded companies for a period matching the expected term assumption and the historical and implied volatility of our stock. The risk-free interest rate, expected volatility, and expected term assumptions depend on the estimated timing of our phase 1 clinical trial for our product candidate utilizing the know-how, biological materials, and intellectual property licensed under the MSKCC Agreement and the U.S. Food and Drug Administration ("FDA") approval of this product candidate. In addition, we incorporated the estimated number and timing of valuation measurement dates in the calculation of the MSKCC success payments liability.

A small change in the assumptions and other inputs, such as the fair value of our common stock, may have a relatively large change in the estimated valuation and associated liability and expense or income.

The carrying value of the promissory note pursuant to the Paycheck Protection Program ("PPP") administered by the Small Business Administration (the "SBA") under the Coronavirus Aid, Relief and Economic Security Act (the "CARES Act") approximated its fair value as of December 31, 2020 (Note 8). On May 22, 2021, our PPP Loan was forgiven in full by the SBA.

4. Significant Agreements

The Regents of the University of California and the University of Vienna

We entered into an Exclusive License Agreement, dated April 16, 2013 (as amended, the "UC/Vienna Agreement") with The Regents of the University of California ("UC") and the University of Vienna ("Vienna") (together, "UC/Vienna") wherein UC/Vienna granted us an exclusive worldwide license, with the right to sublicense, in all fields to the foundational CRISPR-Cas9 patent family co-owned by UC, Vienna, and Dr. Emmanuelle Charpentier (the "CVC IP"). Dr. Charpentier has not granted us any rights, either directly or indirectly. The UC/Vienna Agreement continues until the last-to-expire patent or last-to-be-abandoned patent application within the CVC IP; provided, however, that UC/Vienna may terminate the UC/Vienna Agreement upon the occurrence of certain events and we may terminate the UC/Vienna Agreement at our sole discretion upon written notice. Without patent term adjustment or patent term extension, the CVC IP will expire in 2033. The UC/Vienna Agreement includes certain diligence milestones that we must meet. For products and services sold by us that are covered by the CVC IP, we will owe low- to mid-single-digit percent royalties on net sales, subject to a minimum annual royalty. Prior to the time that we are selling products, we owe UC/Vienna an annual license maintenance fee. We may owe UC/Vienna up to $3.4 million in certain regulatory and clinical milestone payments in the field of human therapeutics and diagnostics for products that are covered by the CVC IP and developed by us, an affiliate, or a sublicensee. Additionally, we pay UC/Vienna a specified percentage of sublicensing revenue, including cash and equity, we receive from sublicensing the CVC IP, subject to certain exceptions. If we include intellectual property owned or controlled by us in a sublicense to the CVC IP, we pay UC/Vienna a low double-digit percentage of sublicensing revenues received under the sublicense. If we do not include intellectual property owned or controlled by us in a sublicense to the CVC IP, we pay UC/Vienna 50% of sublicensing revenues received under the sublicense. To date, we have entered into over 20 sublicensing agreements in a variety of fields such as human therapeutics, forestry, agriculture, research reagents, transgenic animals, certain livestock targets, internal research, bioproduction, cell lines, and microbial applications that include the CVC IP as well as other Cas9 intellectual property owned or controlled by us. We are obligated to reimburse UC for its prosecution and maintenance costs of the CVC IP.

For the years ended December 31, 2021, 2020, and 2019 we incurred $1.5 million, $0.8 million, and $0.8 million, respectively, for payments we owe to UC related to sublicensing revenues, which we recorded in research and development expenses in our consolidated statements of operations and comprehensive loss.

For the years ended December 31, 2021, 2020, and 2019 we reimbursed UC $10.5 million, $9.2 million, and $6.7 million, respectively, for prosecution and maintenance costs of the CVC IP, which we recorded in general and administrative expenses in our consolidated statements of operations and comprehensive loss.

On December 15, 2016, we entered into a Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement ("IMA") relating to the CVC IP. Under the IMA, CRISPR Therapeutics AG ("CRISPR") reimburses us 50% of the amounts we reimburse UC for patent prosecution and maintenance costs of the CVC IP. For the years ended December 31, 2021, 2020, and 2019, CRISPR reimbursed us $5.2 million, $4.2 million, and $3.1 million, respectively, which we recorded as reductions of general and administrative expenses in our consolidated statements of operations and comprehensive loss.

Memorial Sloan Kettering Cancer Center

Under the MSKCC Agreement, we exclusively licensed know-how, biological materials, and intellectual property relating to humanized single-chain variable fragments targeting CD371 for use in T cells, NK cells, and genome-edited induced pluripotent stem cells for allogeneic CD371-targeted cell therapy (currently used in our CB-012 product candidate). We paid MSKCC an upfront payment of $0.5 million in cash and $2.1 million in stock. For each licensed CD371 product, we may owe potential clinical, regulatory, and commercial milestone payments totaling $112.0 million. In addition, in the event we, our affiliates, or sublicensees, receive regulatory approval for a licensed CD371 product, we will owe low- to mid-single-digit percent royalties on net sales by us, our affiliates, and our sublicensees. Our license from MSKCC includes the right to sublicense through multiple tiers and we will owe MSKCC a percentage of upfront cash or equity received from our sublicensees. The percentage owed decreases as our licensed CD371 product candidate moves through development, starting at a low-double-digit percentage if clinical trials have not yet begun and decreasing to a mid-single-digit percentage if our licensed CD371 product candidate is in later clinical trial stages. We are also responsible for paying a percentage of licensed patent costs. The MSKCC Agreement includes certain diligence milestones that we must meet by specified dates, which may be extended upon payment of additional fees.

MSKCC is entitled to certain success payments if our common stock fair value increases by certain multiples of increasing value based on a comparison of the fair market value of our common stock to $5.1914 per share, adjusted for any future stock splits (the "Initial Share Price"), during a specified time period. Under the MSKCC Agreement, as a publicly traded company, our common stock fair value is determined by any given 45-day volume weighted-average trading price. At our option, success payments to MSKCC may be made in cash or common stock. The relevant time period commences when the first patient is dosed with a licensed CD371 product candidate in the first phase 1 clinical trial and ends upon the earlier of the third anniversary from the approval of our, or our affiliate's, or sublicensee's, biologics license application by the FDA or 10 years from the date the first patient was dosed with a licensed CD371 product candidate in the first phase 1 clinical trial. The aggregate success payments will not exceed $35.0 million. Additionally, if we undergo a change of control during the specified time period, we may owe a change of control payment, depending upon the increase in our stock price due to the change of control and also to what extent success payments have already been paid by us to MSKCC. In no event will the combination of success payments and the change of control payment owed to MSKCC exceed $35.0 million.

The following table summarizes the amounts of the MSKCC success payments:

Multiple of Initial Share Price giving rise to a success payment	5x	10x	15x
MSKCC success payments (in millions)	$ 10.0	$ 10.0	$ 15.0

We may terminate the MSKCC Agreement upon 90 calendar days' prior written notice to MSKCC. MSKCC may terminate the MSKCC Agreement in the event of our uncured material breach, bankruptcy, or criminal activity. If MSKCC materially breaches the MSKCC Agreement in certain circumstances (e.g., granting a third party a license in our field) then, during the time of such uncured breach, MSKCC will not be entitled to receive any success payments or any change of control payment.

As of December 31, 2021 and 2020, the estimated fair value of the total success payments obligation to MSKCC was $4.1 million and $2.7 million, respectively, which was included in long-term liabilities in our consolidated balance sheets. The change in fair value from the issuance date to December 31, 2020 was not significant to our consolidated financial statements. For the year ended December 31, 2021, we recognized $1.4 million of change in fair value of the MSKCC success payments liability, which was recorded in other income (expense) in our consolidated statements of operations and comprehensive loss.

Intellia Therapeutics, Inc.

On July 16, 2014, we entered into a License Agreement (as amended, the "Intellia License Agreement") and a Services Agreement with Intellia, LLC, to which Intellia Therapeutics, Inc. ("Intellia") is a successor in interest. Under the Intellia License Agreement, we granted Intellia an exclusive worldwide license, with the right to sublicense, to certain CRISPR-Cas9 technology for a defined field of human therapeutics, including a license to certain of our future CRISPR-Cas9 intellectual property until our direct or indirect percentage of Intellia's common stock dropped below 10% (the "IP Cut-off Date"). Intellia granted us an exclusive worldwide license, with the right to sublicense, to certain of its CRISPR-Cas9 technology for all fields outside of the defined field of human therapeutics, including a license to certain of Intellia's future CRISPR-Cas9 intellectual property until the IP Cut-off Date. Each party had the right to opt in to any licenses in its field of use entered into by the other party prior to the IP Cut-off Date, subject to the terms and conditions of the license. The IP Cut-off Date occurred on January 30, 2018. Under the Intellia License Agreement, each party is responsible for 30% of the other party's expenses for prosecution and maintenance of the licensed intellectual property. For each of the years ended December 31, 2021, 2020, and 2019 we reimbursed Intellia less than $0.1 million, which was recorded as general and administrative expenses in our consolidated statements of operations and comprehensive loss. During each of the years ended December 30, 2021, 2020, and 2019 Intellia reimbursed us $1.9 million, $1.5 million, and $1.2 million, respectively (including reimbursement for a portion of the patent prosecution and maintenance costs of the CVC IP paid to UC), which were recorded as reductions of general and administrative expenses in our consolidated statements of operations and comprehensive loss. The term of the Intellia License Agreement continues for the life of the licensed patents and patent applications; provided, however, either party may terminate the agreement upon the occurrence of certain events.

On June 16, 2021, we entered into a leaseback agreement with Intellia (the "Leaseback Agreement"). Pursuant to the Leaseback Agreement, in exchange for Intellia's grant to us of an exclusive license to certain intellectual property relating to CRISPR-Cas9, including Cas9 chRDNAs, for use solely in the manufacture of our CB-010 product candidate, we paid Intellia an upfront cash payment of $1.0 million and will pay up to $23.0 million in potential future regulatory and sales milestones. Additionally, we will owe Intellia low- to mid- single-digit percent royalties on net sales of our CB-010 product candidate by us, our affiliates, and sublicensees until the expiration, abandonment, or invalidation of the last patent within the intellectual property relating to CRISPR-Cas9, including that relating to Cas9 chRDNAs (i.e., 2036, without patent term adjustment or patent term extension).

Pioneer Hi-Bred International, Inc. (now Corteva Agriscience)

On July 13, 2015, we and Pioneer Hi-Bred International, Inc. ("Pioneer") (now Corteva Agriscience), then a DuPont company ("DuPont"), entered into an Amended and Restated Collaboration and License Agreement, as amended (the "Pioneer Agreement"). Under the terms of the Pioneer Agreement, we and Pioneer cross ―licensed CRISPR intellectual property portfolios. Pioneer granted us an exclusive worldwide license, with the right to sublicense, to its CRISPR intellectual property in the field of research tools, as well as a non-exclusive worldwide license to such intellectual property in human and animal therapeutics, industrial biotechnology, certain agriculture segments, and other fields; and we granted Pioneer an exclusive worldwide license, with the right to sublicense, to our CRISPR intellectual property, including the CVC IP, in a defined field of agriculture relating to specified row crops, as well as a non-exclusive worldwide license to the intellectual property in other agricultural applications, industrial biotechnology, nutrition and health, and other fields. The Pioneer Agreement continues until the expiration, abandonment, or invalidation of the last patent or patent application within the licensed intellectual property; provided, however, that the parties may terminate the Pioneer Agreement by mutual consent or either party may unilaterally terminate the Pioneer Agreement in the event of an uncured breach of a payment obligation, bankruptcy, or failure to maintain or own licensed intellectual property by the other party if the non-breaching party is materially adversely affected by the failure. We are obligated to pay low-single-digit percent royalties to Pioneer for the sales of our products in the research tools field as well as certain sublicensing revenues in that field. We are eligible to receive milestone payments from Pioneer if certain regulatory and commercial milestones are met related to specified row crops, for a total of up to $22.4 million, as well as to receive low-single-digit percent royalties for sales of defined agricultural products and certain sublicensing revenues in that field. In March 2021, we received a milestone payment of $0.3 million from Pioneer. Under the Pioneer Agreement, we and Pioneer also entered into a three-year collaboration, funded by Pioneer, which ended in 2016. Initially, Pioneer owned the patents and patent applications developed under the collaboration, including the chRDNA patent family, and granted us an exclusive license to these patents and patent applications in the fields of research tools and therapeutics.

In December 2020, we and Pioneer entered into an amendment to the Pioneer Agreement under which Pioneer assigned to us the chRDNA patent family developed under the research collaboration, and we paid Pioneer an upfront payment of $0.5 million. We considered the payment to Pioneer in accordance with revenue recognition guidance and accounted for it as a reduction of the licensing and collaboration revenue in our consolidated statements of operations and comprehensive loss. In addition to the upfront payment, we are now obligated to pay all patent prosecution and maintenance costs for the chRDNA patent family; up to $2.8 million in regulatory milestone payments for therapeutic products developed by us, our affiliates, or licensees that are covered by the chRDNA patent family; up to $20.0 million in sales milestones over a total of four therapeutics products sold by us, our affiliates, or

licensees that are covered by the chRDNA patent family; and a low-single-digit percentage of licensing revenue we receive for licensing the chRDNA patent family after December 2020.

During the year ended December 31, 2021, we incurred $0.8 million for payments we owe to Pioneer related to licensing revenues, which we recorded as a research and development expense in our consolidated statements of operations and comprehensive loss. No licensing fees payments were incurred to Pioneer during the years ended December 31, 2020 and 2019.

Genus plc

On May 12, 2016, we entered into a Research Collaboration and License Agreement (as amended, the "Genus Agreement") with Genus plc ("Genus") under which we granted Genus an exclusive worldwide license to certain CRISPR-Cas9 technology for the introduction of genetic traits into cattle and pigs raised to produce protein primarily for human consumption; provided, however, that at the end of the four-year research collaboration, Genus was required to select a specified number of licensed products and our license to Genus is now limited to those particular products. The Genus Agreement continues until the expiration, abandonment, or invalidation of the last patent or patent application within the licensed patent rights; provided, however, that each party may terminate the Genus Agreement upon the occurrence of certain events, and Genus may terminate the Genus Agreement at its sole discretion upon written notice to us. In addition to an upfront payment we received, we are eligible to receive milestone payments from Genus if certain regulatory and commercial milestones are met, for the selected licensed products, up to a total of $10.0 million. We will also be eligible to receive either low- to mid-single-digit percent royalties or low-single to low-double-digit percent royalties on net sales of the licensed products.

Under the Genus Agreement, we and Genus entered into a four-year research collaboration, which was funded by Genus. The collaboration ended in May 2020. We did not recognize any revenue in connection with the Genus Agreement for the year ended December 31, 2021. During the years ended December 31, 2020 and 2019, we recognized revenue of $0.8 million and $2.3 million, respectively, related to the Genus Agreement.

Private Company, Related Party

On May 15, 2020, we entered into an Exclusive License Agreement, as amended, with a private company, related party (the "Private Company License Agreement"), under which we granted the private company an exclusive worldwide license to certain CRISPR intellectual property rights and know-how in a defined field.

We are eligible to receive milestone payments for licensed products following the first commercial sale of each licensed product in each of the United States and the first European country in which each licensed product is sold by the private company. The private company may select one of several milestone payment amounts for each licensed product; the selection of which dictates the applicable royalty rate for net sales of licensed products. We are also eligible to receive a percentage of sublicensing revenues in the event the private company sublicenses the CRISPR intellectual property that we licensed to the private company.

The Private Company License Agreement will continue in force and effect until the expiration, abandonment, or invalidation of the last patent or patent application within the licensed patent rights. The Private Company License Agreement may be terminated during the term by either party for an uncured material breach or bankruptcy. Additionally, the private company may terminate the Private Company License Agreement upon 90 days' written notice to us.

As consideration for the exclusive license, the private company issued to us 7,500,000 shares of convertible preferred stock with an estimated fair value of $7.5 million, which was the price paid for similar shares by another investor, and which was an arm's length transaction. We accounted for the grant of the license as a contract with a customer under ASC 606 and recognized $7.5 million as license and collaboration revenue in our consolidated statements of operations and comprehensive loss for the year ended December 31, 2020. We did not recognize any revenue in connection with the Private Company License Agreement for the year ended December 31, 2021.

On May 15, 2020, we entered into a separate option agreement under which we granted the same private company a three-year option to negotiate an exclusive, royalty-bearing, worldwide license in a defined field to the CVC IP and certain other CRISPR-Cas9 patent rights controlled by us. Through December 31, 2021, we have received a total of $0.1 million in upfront option payments, and we may receive an additional annual option fee and an option exercise fee. We recorded the upfront option payments received in long-term deferred revenue in our consolidated balance sheets as of December 31, 2021 and 2020.

AbbVie Manufacturing Management Unlimited Company

On February 9, 2021, we entered into a Collaboration and License Agreement (the "AbbVie Agreement") with AbbVie Manufacturing Management Unlimited Company ("AbbVie"). Pursuant to the AbbVie Agreement, AbbVie selects one target or, for a dual CAR-T product, two targets (each selection, a "Program Slot") to develop collaboration CAR-T products (and corresponding licensed products). For each of AbbVie's two Program Slots (or up to four Program Slots, if AbbVie elects to expand the number as set forth below), we will collaborate to develop one or more collaboration allogeneic CAR-T products directed toward the single cancer target or target combination chosen by AbbVie as described in an applicable research plan, utilizing our Cas12a chRDNA genome-editing and cell therapy technologies. We granted AbbVie an exclusive (even as to us), royalty-bearing, worldwide license, with the right to grant sublicenses, under our Cas12a chRDNA and cell therapy intellectual property, as well as certain genome-editing technology that we may gain rights to in the future and intellectual property that may be developed under the collaboration, solely for AbbVie to develop, commercialize, manufacture, and otherwise exploit the collaboration CAR-T products in the field of human diagnostics, prophylactics, and therapeutics. Under the terms of the AbbVie Agreement, we conduct certain preclinical research, development, and manufacturing activities under the collaboration, including certain activities for the manufacture and supply of licensed product for AbbVie's phase 1 clinical trials. AbbVie reimburses us for all such activities, including reimbursement for time spent by employees at a designated FTE rate. The duration of the collaboration is not fixed. Under the terms of the AbbVie Agreement, AbbVie has selected its initial Program Slot and has reserved six additional targets, which AbbVie may choose to be used or substituted into the two Program Slots or used for the third or fourth Program Slots if AbbVie expands the number of Program Slots during the collaboration.

During the collaboration, AbbVie may expand from two Program Slots to a total of four Program Slots by paying us an additional $15.0 million for each Program Slot, provided that AbbVie must make such payment within the earlier of (i) 60 calendar days following completion of the phase 1 clinical trials for the initial collaboration CAR-T and (ii) December 31, 2025. Under the terms of the AbbVie Agreement, we are eligible to receive up to $150.0 million in future developmental and regulatory milestone payments for each Program Slot and up to $200.0 million in sales-based milestones for each Program Slot. We are also eligible to receive global royalties on net sales of licensed products sold by AbbVie, its affiliates, and sublicensees in the high-single-digit to low-teens percent range, subject, in certain instances, to various reductions.

The term of the AbbVie Agreement will continue in force and effect until the date of expiration of the last royalty term of the last country in which a licensed product is exploited. On a licensed product-by-licensed product and country-by-country basis, the royalty term is the period of time beginning on the first commercial sale of a licensed product in a country and ending on the latest of the following three dates: (i) the expiration, invalidation, revocation, cancellation, or abandonment date of the last patent that includes a valid claim to either (A) the collaboration CAR-T product in the licensed product or (B) the method of making the collaboration CAR-T product in the licensed product in such country (in the case of (B), only for so long as no biosimilar product is commercially available in such country); (ii) 10 years from the date of the first commercial sale of such licensed product in such country; and (iii) the expiration date of regulatory exclusivity for such licensed product in such country. The AbbVie Agreement may be terminated during the term by either party for an uncured material breach or bankruptcy by the other party. Additionally, AbbVie may terminate the AbbVie Agreement, in its entirety or on a licensed product-by-licensed product basis, effective immediately upon written notice to us, if AbbVie in good faith believes that it is not advisable for AbbVie to continue to exploit the collaboration CAR-T products or licensed products as a result of a perceived serious safety issue. AbbVie may also terminate the AbbVie Agreement in its entirety at its sole discretion upon 90 days' prior written notice to us.

The transaction price we received under the AbbVie Agreement associated with the first two Program Slots consisted of a $30.0 million upfront cash payment and the estimated variable consideration related to our performance of preclinical, development, and manufacturing activities under the collaboration and the developmental and regulatory milestone payments. We constrain the estimated variable consideration if we assess that it is probable that a significant reversal in the amount of cumulative revenue recognized may occur in future periods. We constrained all developmental and regulatory milestone payments as of December 31, 2021. The transaction price will be reevaluated in each reporting period and as changes in circumstances occur. We determined that the licenses we granted to AbbVie and our participation in the joint governance committee are not capable of being distinct from the preclinical research, development, and manufacturing activities and therefore are combined into one performance obligation. We recognize revenue based on the measure of progress using an estimated cost-based input method each reporting period.

We received an upfront cash payment of $30.0 million and $0.2 million in expenses reimbursements from AbbVie during the year ended December 31, 2021. We recognized short-term deferred revenue in the amount of $8.3 million and long-term deferred revenue in the amount of $19.1 million related to these payments in our consolidated balance sheets as of December 31, 2021. We recognized $4.0 million in revenue for the year ended December 31, 2021 in relation to the AbbVie Agreement. As of December 31, 2021, we also recorded $1.0 million in accounts receivable and $0.2 million in contract assets in our consolidated balance sheets.

5. Revenue

Disaggregation of Revenue

We disaggregate revenue by geographical market based on the location of research and development activities of our licensees and collaborators. The following is a summary of revenue by geographic location for the years ended December 31, 2021, 2020, and 2019 (in thousands):

	Years Ended December 31,		
	2021	2020	2019
United States	$ 8,913	$ 12,003	$ 5,349
Rest of world	685	358	439
Total	$ 9,598	$ 12,361	$ 5,788

During the year ended December 31, 2021, we recognized $5.6 million of revenue related to performance obligations satisfied at a point in time, and we recognized $4.0 million of revenue related to performance obligations satisfied over time.

During the year ended December 31, 2020, we recognized $11.6 million of revenue related to performance obligations satisfied at a point in time, and we recognized $0.8 million of revenue related to performance obligations satisfied over time.

During the year ended December 31, 2019, we recognized $3.5 million of revenue related to performance obligations satisfied at a point in time, and we recognized $2.3 million of revenue related to performance obligations satisfied over time.

Contract Balances

Accounts receivable relate to our right to consideration for performance obligations completed (or partially completed) for which we have an unconditional right to consideration. Our accounts receivable balances represent amounts that we billed to licensees with invoices outstanding as of the period end.

Contract assets are rights to consideration in exchange for a license that we have granted to a licensee when the right is conditional on something other than the passage of time. Our contract asset balances represent royalties, milestone payments, and research costs related to the AbbVie Agreement that are unbilled as of the period end.

Contract liabilities consist of deferred revenue and relate to amounts invoiced to, or advance consideration received from, licensees, which precede our satisfaction of the associated performance obligations. Our deferred revenue primarily results from upfront payments received relating to performance obligations that are satisfied over time under the AbbVie Agreement. The remaining deferred revenue relates to upfront payments received under license agreements that also include non-refundable annual license fees, which are accounted for as material rights for license renewals and are recognized at the point in time the annual license fee is paid by the licensee and the renewal period begins.

The following table presents changes in our contract assets and liabilities during the year ended December 31, 2021 (in thousands):

	Balance as of December 31, 2020	Additions	Deductions	Balance as of December 31, 2021
Accounts receivable	$ 150	$ 9,105	$ (8,102)	$ 1,153
Contract assets:				
Unbilled accounts receivable	$ 1,328	$ 5,144	$ (4,984)	$ 1,488
Contract liabilities:				
Deferred revenue, current and long-term	$ 1,098	$ 35,022	$ (5,385)	$ 30,735

Unbilled accounts receivable increased during the year ended December 31, 2021, primarily due to increases of $0.2 million in our right to consideration related to earned royalties not billed and $0.2 million of unbilled research costs under the AbbVie Agreement, offset by a decrease of $0.3 million in regulatory milestone for Pioneer.

Deferred revenue increased during the year ended December 31, 2021, primarily due to recognition of $30.0 million in deferred revenue related to the AbbVie Agreement (Note 4).

During the years ended December 31, 2021, 2020, and 2019, we recognized $0.1 million, $0.7 million, and $1.8 million of revenue, respectively, which were included in the opening contract liabilities balances as of January 1, 2021, 2020, and 2019, respectively.

Transaction Prices Allocated to the Remaining Performance Obligations

Remaining unsatisfied performance obligations represent in aggregate the amount of a transaction price that has been allocated to performance obligations not delivered as of the end of a reporting period. The value of transaction prices allocated to remaining unsatisfied performance obligations as of December 31, 2021 and 2020 were approximately $46.0 million and $1.1 million, respectively. We expect to recognize approximately $8.7 million of remaining performance obligations as revenue in the next 12 months, and the remainder thereafter.

Capitalized Contract Acquisition Costs and Fulfillment Costs

We did not incur any expenses to obtain license and collaboration agreements, and costs to fulfill those contracts do not generate or enhance our resources. As such, no costs to obtain or fulfill a contract have been capitalized in any period.

6. Balance Sheet Items

Other receivables consisted of the following as of December 31, 2021 and 2020 (in thousands):

	December 31, 2021	December 31, 2020
Patent cost reimbursements	$ 4,702	$ 3,672
Accrued interest on marketable securities	226	—
Other	555	10
Total	$ 5,483	$ 3,682

Prepaid expenses and other current assets consisted of the following as of December 31, 2021 and 2020 (in thousands):

	December 31, 2021	December 31, 2020
Prepaid income taxes	$ 2,714	$ 954
Prepaid insurance	1,897	—
Prepaid contract manufacturing and clinical costs	1,486	1,479
Prepaid rent	468	337
Other	671	423
Total	$ 7,236	$ 3,193

Property and equipment, net, consisted of the following as of December 31, 2021 and 2020 (in thousands):

	December 31, 2021	December 31, 2020
Lab equipment	$ 6,848	$ 5,038
Leasehold improvements	1,701	1,180
Computer equipment	273	263
Furniture and equipment	133	117
Construction in progress	9	—
Total property and equipment, gross	8,964	6,598
Less: accumulated depreciation and amortization	(4,077)	(3,096)
Property and equipment, net	$ 4,887	$ 3,502

Depreciation and amortization expenses related to property and equipment were $1.0 million, $0.9 million, and $0.8 million for the years ended December 31, 2021, 2020, and 2019, respectively.

Accrued expenses and other current liabilities consisted of the following as of December 31, 2021 and 2020, respectively (in thousands):

	December 31, 2021	December 31, 2020
Accrued personnel-related expenses	4,225	2,081
Accrued research and development expenses	4,065	581
Accrued patent expenses	3,213	5,087
Accrued sublicensing fees	586	402
Credit card liability	259	193
Other	788	629
Total	$ 13,136	$ 8,973

7. Related Party Transactions

Private Company, Related Party

On May 15, 2020, we received 7,500,000 shares of convertible preferred stock with an estimated fair value of $7.5 million as consideration for the Private Company License Agreement (Note 4). This represents a material voting interest in the private company and entitles us to hold one of the four private company's board of director seats and to jointly vote with another stockholder on a second board of director seat. As of December 31, 2021, we have appointed one of the three directors on the private company board of directors. We concluded that the private company is a variable interest entity and that we are not its primary beneficiary based on our representation on its board of directors. As the private company's convertible preferred stock is not in substance common stock, we record this investment using the measurement alternative in accordance with ASC 321, Investments - Equity Securities. Under the measurement alternative, our investment in the private company's convertible preferred stock was initially recorded at its estimated fair value, but the carrying value may be adjusted through earnings upon an impairment or when there is an observable price change involving the same or a similar investment with the private company. As of each of December 31, 2021 and 2020, the carrying value of investment was $7.5 million. There have been no changes to the carrying value of the investment during the years ended December 31, 2021 and 2020.

Pioneer

As of December 31, 2020, DuPont held a greater than 10% voting interest in the Company and Pioneer, then a DuPont company, was considered a related party (Note 4). Upon the closing of our IPO in July 2021, and as of December 31, 2021, DuPont had a voting interest exceeding 5% in us and Pioneer was considered a related party.

Scientific Advisory Board Member Payments

Dr. Jennifer A. Doudna, a co-founder and stockholder of the Company, receives compensation for participating on our scientific advisory board (the "SAB"). During the year ended December 31, 2021, we paid Dr. Doudna $0.1 million. During the years ended December 31, 2020, and 2019, we paid Dr. Doudna less than $0.1 million for her participation on our SAB.

Loan to our President and Chief Executive Officer

In November 2018, our president and chief executive officer entered into a promissory note with us for $1.1 million, as a means to provide liquidity without triggering a taxable event. The note bore interest at a rate of 3.04%, compounded annually, and was payable in five years, together with principal and accrued interest. The promissory note was secured by 409,795 shares of our common stock owned by our president and chief executive officer and was determined to be non-recourse for accounting purposes. As such, the issuance of the promissory note was effectively the grant of a new share option. The promissory note was repaid in full amount in June 2021 by our president and chief executive officer and recognized as an increase in additional paid in capital of $1.2 million.

8. Paycheck Protection Program Loan

On May 6, 2020, we entered into a promissory note with WebBank (the "Lender") pursuant to the Paycheck Protection Program for a total amount of $1.6 million (the "PPP Loan").

Our PPP Loan had a two-year term and bore interest at a stated rate of 1.0% per annum, accrued monthly, beginning on the date our PPP Loan was issued by the Lender. No monthly principal and interest payments were required under our PPP Loan.

We did not provide any collateral or guarantees for our PPP Loan, nor did we pay any facility charge to obtain our PPP Loan. Our PPP Loan provided for customary events of default, including those relating to failure to make payment, bankruptcy, breaches of representations, and material adverse effects. We could have prepaid the principal of our PPP Loan at any time without incurring any prepayment charges.

A PPP loan can be partially or fully forgiven if a borrower complies with the provisions of the CARES Act, including the use of PPP loan proceeds for payroll costs, rent, utilities, and certain other expenses, and at least 60% of the PPP loan proceeds must be used for payroll costs as defined by the CARES Act. Any forgiveness of a PPP loan is subject to approval by the SBA.

On May 22, 2021, our PPP Loan was forgiven in full by the SBA and, at that time, we recognized a PPP Loan extinguishment gain of $1.6 million in our consolidated statements of operations and comprehensive loss.

9. Commitments and Contingencies

Facility Lease Agreements

We lease laboratory and office space under non-cancellable operating agreements. On March 31, 2021, we entered into a ten-year lease agreement, which superseded and replaced our prior lease, as amended, and the lease included additional office and laboratory space located within the same building in Berkeley, California. Our lease agreement contains a renewal option for an additional term of five years. Monthly base rent under our lease agreement amounts to $0.3 million, subject to annual escalation from 3.1% to 3.5%. In addition to base rent, we pay our share of operating expenses and taxes. Our rent commitments under these leases are $3.5 million within the next 12 months from December 31, 2021, and $38.3 million for the remainder of the lease terms.

We record rent expense on a straight-line basis over the term of our leases. For tenant improvement allowances funded by landlord incentives, we record a deferred lease incentive liability in accrued expenses and other liabilities and amortize the deferred lease incentive liability as a reduction to rent expense in our consolidated statements of operations and comprehensive loss over the term of the applicable lease. As of December 31, 2021 and 2020, we recorded $0.8 million and $0.6 million, respectively, related to the required security deposits in other assets, long-term, in our consolidated balance sheets.

As of December 31, 2021, future minimum lease payments under the leases were as follows (in thousands):

2022	$	3,485
2023		3,596
2024		3,708
2025		3,627
2026		4,838
Thereafter		22,541
Total	$	41,795

Rent expense was $4.0 million, $2.5 million, and $1.6 million for the years ended December 31, 2021, 2020, and 2019, respectively.

Capital Lease

We accounted for certain leased equipment as a capital lease due to the ownership of such equipment transferring to us at the end of the lease term. As of December 31, 2021, the capital lease obligation was repaid in full and we do not have any remaining future minimum lease payments related to this capital lease. As of December 31, 2020, the total capital lease obligation amounted to $0.1 million, which was included in the current portion of the capital lease obligation in the accrued expenses and other current liabilities and the non-current portion of the capital lease in other liabilities in our consolidated balance sheets.

Research and Development Agreements

We enter into various agreements in the ordinary course of business, such as those with suppliers, CROs, CMOs, clinical trial sites, and the like. These agreements provide for termination at the request of either party, generally with less than one-year notice and are, therefore, cancellable contracts and, if canceled, are not anticipated to have a material effect on our consolidated financial condition, results of operations, or cash flows.

Guarantees and Indemnifications

In the normal course of business, we enter into agreements that contain a variety of representations and warranties and provide for certain indemnifications by us. Our exposure under these agreements is unknown because claims may be made against us in the future. To date, we have not paid any claims or been required to defend any action related to our indemnification obligations. As of each of December 31, 2021 and 2020, we did not have any material indemnification claims that were probable or reasonably possible, and consequently, we have not recorded related liabilities.

Intellia Arbitration

In October 2018, Intellia initiated an arbitration proceeding with JAMS, asserting that we had violated the terms and conditions of the Intellia Agreement (the "Intellia Arbitration"). The Intellia Arbitration focused on whether two patent families controlled by us and respectively, to CRISPR-Cas9 chRDNAs and Cas9 scaffolds are included in the Intellia Agreement. In September 2019, the parties received an interim award from the arbitration panel ruling that the two patent families are included in the Intellia Agreement, but the arbitration panel granted us an exclusive leaseback to Cas9 chRDNAs under economic terms to be negotiated by the parties. In February 2020, the arbitration panel clarified that the leaseback relates solely to our CB-010 program and instructed the parties to negotiate economic terms based on a leaseback of that scope (Note 4). On June 16, 2021, the parties entered into the Leaseback Agreement, which resolved the dispute and, on July 21, 2021, the arbitration panel dismissed the Intellia Arbitration with prejudice.

Litigation

From time to time, we may become involved in legal proceedings arising in the ordinary course of business. We record a liability for such matters when it is probable that future losses will be incurred and if such losses can be reasonably estimated. Significant judgment by us is required to determine both probability and the estimated amount. We do not believe that there is any litigation or asserted or unasserted claim pending that could, individually or in the aggregate, have a material adverse effect on our results of operations or financial condition.

10. Convertible Preferred Stock

The authorized, issued, and outstanding shares of our convertible preferred stock and liquidation preferences as of December 31, 2020 were as follows (in thousands, except for share amounts):

Series	Authorized Shares	Outstanding Shares	Liquidation Preference	Carrying Value
Series A	1,576,342	1,576,342	$ 3,550	$ 3,452
Series A-1	3,004,124	3,004,124	8,000	7,901
Series B	3,186,116	3,186,116	30,070	29,970
	7,766,582	7,766,582	$ 41,620	$ 41,323

In connection with the closing of our IPO on July 27, 2021, all outstanding shares of convertible preferred stock, including the Series C preferred stock issued in March 2021, were converted into shares of common stock. Our amended and restated certificate of Incorporation, which was approved by the board of directors and stockholders in connection with our IPO, authorizes the issuance of 10,000,000 shares of preferred stock with par value of $0.0001 upon the closing of our IPO. None of the preferred stock was issued and outstanding as of December 31, 2021.

11. Common Stock

Common stock reserved for future issuance, on an as-converted basis, consists of the following:

	As of December 31, 2021	As of December 31, 2020
Preferred stock, issued and outstanding	—	14,119,631
Stock options, issued and outstanding	6,757,591	4,520,551
Stock options, authorized for future issuance	3,749,339	582,340
Stock available under the Employee Stock Purchase Plan	511,000	—
Restricted stock awards	—	5,999
	11,017,930	19,228,521

12. Equity Compensation Plans

In July 2021, our board of directors adopted and our stockholders approved the 2021 Equity Incentive Plan (the "2021 Plan") that became effective on July 22, 2021. We reserved 5,200,000 shares of common stock for issuance under the 2021 Plan. In addition, 934,562 shares available for issuance under the 2013 Equity Incentive Plan, adopted in 2013 and amended and restated in 2019, were transferred into the 2021 Plan. Furthermore, any shares subject to awards under the 2013 Plan that terminate, expire, or lapse for any reason without the delivery of shares, or are reacquired or withheld (or not issued) to satisfy a tax withholding obligation or the purchase or exercise price, will be added to the 2021 Plan. The 2021 Plan also provides that the number of shares initially reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2022 and ending on January 1, 2031, by an amount equal to the lesser of (i) 5% of the shares of common stock outstanding on the last day of the immediately preceding fiscal year, and (ii) such smaller number of shares of stock as determined by our Board. No more than 56,000,000 shares of stock may be issued upon the exercise of incentive stock options under the 2021 Plan. Options under the 2021 Plan may be granted for periods of up to 10 years at exercise prices no less than the fair market value of our common stock on the date of grant; provided, however, that the exercise price of an incentive stock option granted to a 10% stockholder may not be less than 110% of the fair market value of the shares on the date of grant and such option may not be exercisable after the expiration of five years from the date of grant. The grant date fair market value of all awards made under our 2021 Plan and all cash compensation paid by us to any non-employee director for services as a director in any fiscal year may not exceed $750,000, increased to $1,000,000 in the fiscal year of their initial service as a non-employee director. As of December 31, 2021, we had 3,749,339 shares available for issuance under our 2021 Plan.

The following table summarizes stock option activity under our equity incentive plans during the year ended December 31, 2021:

	Shares Available to Grant	Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands) (a)
Outstanding at December 31, 2020	582,340	4,520,551	$ 1.64	5.3	$ 6,929
Addition—option pool	7,871,714				
Options granted	(4,860,623)	4,860,623	$ 10.99	9.6	
Options exercised	—	(2,467,675)	$ 1.04		
Options cancelled or forfeited	155,908	(155,908)	$ 2.39		
Outstanding at December 31, 2021	3,749,339	6,757,591	$ 8.57	8.7	$ 50,085
Exercisable at December 31, 2021		1,295,411	$ 2.34	5.9	$ 16,519
Vested and expected to vest at December 31, 2021		6,757,591	$ 8.57	8.7	$ 50,085

(a) The aggregate intrinsic value is calculated as the difference between the stock option exercise price and the estimated fair value of the underlying common stock as of December 31, 2021.

Grant Date Fair Value

During the year ended December 31, 2021, we granted 4,860,623 stock options to employees and non-employees with a weighted-average grant date fair value of $7.39.

During the year ended December 31, 2020, we granted 509,820 stock options to employees and non-employees with a weighted-average grant date fair value of $1.82.

We estimated the fair value of each employee and non-employee stock option award on the grant date using the Black-Scholes option-pricing model based on the following assumptions for the years ended December 30, 2021, 2020, and 2019:

	Years Ended December 31,		
	2021	2020	2019
Volatility	71.5% to 76.5%	72.0% to 76.8%	70.3% to 70.7%
Expected term (in years)	5.5 to 7.0	5.5 to 10.0	6.0 to 9.4
Risk-free interest rate	0.9% to 1.6%	0.3% to 0.7%	1.9%
Expected dividend yield	0.0%	0.0%	0.0%

As of December 31, 2021, there was $34.5 million of unrecognized stock-based compensation expense related to employee and non-employee stock options that is expected to be recognized over a weighted-average period of 3.1 years.

Employee Stock Purchase Plan

In July 2021, our board of directors adopted and our stockholders approved the ESPP, which became effective on July 22, 2021. The ESPP is intended to qualify as an employee stock purchase plan under Section 423 of the Internal Revenue Code of 1986, as amended ("Tax Code"). We reserved 511,000 shares of our common stock for employee purchases under the ESPP. The number of shares of common stock reserved for issuance under the ESPP will be automatically increased each year for 10 calendar years beginning in 2022 by an amount equal to the lesser of (i) 1% of the shares of common stock outstanding on the last day of the immediately preceding fiscal year, and (ii) such smaller number of shares of stock as determined by our Board; provided that the maximum number of shares that may be issued under the ESPP is 10,000,000 shares. The ESPP allows an eligible employee to purchase shares of our common stock at a discount through payroll deductions of up to 15% of the employee's eligible compensation. At the end of each offering period, employees are able to purchase shares at 85% of the lower of the fair market value of our common stock at the beginning of the offering period or at the end of each applicable offering period. The first offering period commenced on August 16, 2021 and will end on February 15, 2022. We recorded $0.3 million in accrued liabilities related to contributions withheld as of December 31, 2021.

Stock-Based Compensation Expense

We recorded stock-based compensation expense related to employee and non-employee stock options grants in our consolidated statements of operations and comprehensive loss for the years ended December 31, 2021, 2020, and 2019 as follows (in thousands):

	Years Ended December 31,		
	2021	**2020**	**2019**
Research and development	$ 1,358	$ 694	$ 597
General and administrative	2,091	308	637
Total	$ 3,449	$ 1,002	$ 1,234

The above stock-based compensation expense related to the following equity-based awards (in thousands):

	Years Ended December 31,		
	2021	**2020**	**2019**
Stock options	$ 3,323	$ 1,002	$ 1,234
ESPP	126	—	—
Total	$ 3,449	$ 1,002	$ 1,234

Stock-based compensation expense related to employees was $3.4 million, $1.0 million, and $1.2 million for the years ended December 31, 2021, 2020, and 2019, respectively. Stock-based compensation expense related to non-employees was less than $0.1 million for each of the years ended December 31, 2021, 2020, and 2019, respectively.

Restricted Stock Awards

In June and October of 2020, our board of directors granted a total of 5,999 restricted stock awards ("RSAs") to a non-employee that vested over a service period of three months. Stock-based compensation expense for RSAs was recognized ratably over the service period and amounted to less than $0.1 million for the year ended December 31, 2020, which was reported within the general and administrative expense in the consolidated statement of operations and comprehensive loss. RSAs were fully vested and outstanding in common stock as of December 31, 2020.

13. 401(k) Savings Plan

In 2017, we established a defined-contribution savings plan under Section 401(k) of the Tax Code. Our 401(k) plan is available to all employees and allows participants to defer a portion of their annual compensation on a pre-tax basis subject to

applicable laws. We also provide a 4% match for employee contributions up to a certain limit. During the years ended December 31, 2021, 2020, and 2019, we contributed $0.4 million, $0.3 million, and $0.3 million, respectively, to our 401(k) plan.

14. Income Taxes

We reported pre-tax book losses in the United States of $66.6 million, $36.1 million, and $31.0 million for the years ended December 31, 2021, 2020, and 2019 respectively.

A reconciliation of the U.S. statutory income tax rate to our effective tax rate is as follows:

Years	2021	2020	2019
Federal income tax (benefit) at statutory rate	(21%)	(21%)	(21%)
State taxes, net of federal benefit	(9%)	(6%)	(4%)
Change in valuation allowance, federal	26%	19%	0%
Change in valuation allowance, state	9%	6%	1%
Stock-based compensation	(1%)	1%	1%
R&D tax credits, net of reserves	(4%)	(3%)	(2%)
Other	0%	(1%)	1%
Effective income tax rate	(0%)	(5%)	(24%)

The 2019 and 2020 effective tax rate reconciliations have been updated to conform to the 2021 presentation.

For the years ended December 31, 2021, 2020, and 2019 our tax provision for (benefit from) income taxes consisted of the following (in thousands):

Years	2021	2020	2019
Current income taxes			
Federal	$ —	$ (907)	$ (404)
State	1	7	(20)
Total current income tax (benefit) expense	1	(900)	(424)
Deferred income taxes:			
Federal	317	(950)	(6,201)
State	3	31	(912)
Total deferred income tax (benefit) expense	320	(919)	(7,113)
Total income tax (benefit) expense	$ 321	$ (1,819)	$ (7,537)

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes.

The following table presents significant components of our deferred tax assets and liabilities as of December 31, 2021 and 2020 (in thousands):

	2021	2020
Deferred tax assets:		
NOL and tax attributes	$ 32,878	$ 10,110
Accrued expenses and reserve	1,055	868
Deferred revenue and expenses	872	505
State income taxes	7	7
Capitalized license and patent costs	1,980	1,493
Stock-based compensation	576	203
Total deferred tax assets	37,368	13,186
Valuation allowance	(34,521)	(10,702)
Net deferred tax assets	2,847	2,484
Deferred tax liabilities:		
Investments in equity securities	(2,077)	(1,866)
Fixed assets	(1,246)	(773)
Total deferred tax liabilities	(3,323)	(2,639)
Net deferred tax assets (liabilities)	$ (476)	$ (155)

We have evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. As of December 31, 2020, a valuation allowance of $10.7 million was recorded against our deferred tax assets. As of December 31, 2021, our deferred tax assets were primarily the result of historical federal and state net operating loss ("NOL") and tax credits, accrued expenses and reserves, and intangible assets capitalized. As of December 31, 2021, a valuation allowance of $34.5 million was recorded against our deferred tax assets.

As of December 31, 2021, we had federal NOL carryforwards of $87.7 million, which do not expire. As of December 31, 2021, we had state NOL carryforwards of $74.2 million, which may be available to offset future state income, and which expire at various years beginning with 2036.

As of December 31, 2021, we generated federal research and development tax credit carryforwards of $6.5 million, which will begin to expire in 2034. As of December 31, 2021, we had state credit carryforwards of $4.2 million available to reduce future tax liabilities, which do not expire.

The CARES Act permits NOL carryovers and carrybacks to offset 100% of taxable income for taxable years beginning before 2021. In addition, the CARES Act allows NOLs incurred in tax years beginning after December 31, 2017 and before January 1, 2021 to be carried back to each of the five preceding taxable years to generate a refund of previously paid income taxes. The income tax benefit recognized in the year ended December 31, 2020 is primarily due to the recognition of NOL carrybacks under the CARES Act, which generated a refund of taxes paid for the year ended December 31, 2018.

Under Section 382 of the Tax Code, the ability to utilize NOL carryforwards or other tax attributes, such as research tax credits, in any taxable year may be limited if we have experienced an "ownership change." Generally, a Section 382 ownership change occurs if there is a cumulative increase of more than 50 percentage points in the stock ownership of one or more stockholders or groups of stockholders who own at least 5% of a corporation's stock within a specified testing period. Similar rules may apply under state tax laws. As a result of our analysis, we believe that there have been three ownership changes under Section 382; however, none of our state NOL and research and development tax credit carryforwards is currently expected to expire unused. We may experience ownership changes as a result of future financing or other changes in the stock ownership.

The following table summarizes the activity related to our unrecognized tax benefits for the three years ended December 31, 2021 (in thousands):

Unrecognized tax benefits—January 1, 2019	$	589
Increases related to current year tax positions		215
Increases related to prior year tax positions		6
Decreases related to lapse of statutes		—
Unrecognized tax benefits—December 31, 2019		810
Increases related to current year tax positions		363
Increases related to prior year tax positions		180
Decreases related to lapse of statutes		—
Unrecognized tax benefits—December 31, 2020		1,353
Increases related to current year tax positions		869
Increases related to prior year tax positions		7
Decreases related to prior year tax positions		(27)
Decreases related to lapse of statutes		—
Unrecognized tax benefits—December 31, 2021	$	2,202

As of December 31, 2021, no amount of unrecognized tax benefits, if recognized, would affect the effective tax rate. We do not expect a significant change to our unrecognized tax benefits over the next 12 months. The unrecognized tax benefits may increase or change during the next year for items that arise in the ordinary course of business.

We recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2021 and 2020, we had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in our consolidated statements of operations and comprehensive loss.

We file our federal and state income tax returns with varying statutes of limitations. Our tax years from 2012 through 2021 will remain open to examination due to the carryover of the unused NOLs and tax credits. There are no ongoing examinations by taxing authorities at this time.

On June 29, 2020, California Assembly Bill 85 (AB 85) was signed into law, which suspends the use of NOLs and limits the use of research tax credits for 2020, 2021, and 2022. There may be periods during which the use of NOLs is suspended or otherwise

limited, and limitation on the use of certain tax credits to offset California income and tax liabilities could accelerate, or permanently increase, state taxes owed. We continue to examine the impact this may have on our business.

On December 27, 2020, the federal "Consolidated Appropriations Act, 2021" was enacted, which includes further COVID-19 economic relief and the extension of certain expiring tax provisions. The relief package included a tax provision clarifying that businesses with forgiven PPP loans can deduct regular business expenses that are paid for with loan proceeds. Additional COVID-19 pandemic relief tax measures included an expansion of the employee retention credit, enhanced charitable contribution deductions, and a temporary full deduction for business expenses for food and beverages provided by a restaurant. These benefits do not have a material impact on our current tax provision.

15. Net Loss Per Share

The following table sets forth the computation of the basic and diluted net loss per share (in thousands, except share and per share amounts):

	Years Ended December 31,		
	2021	2020	2019
Numerator:			
Net loss	$ (66,923)	$ (34,308)	$ (23,431)
Denominator:			
Weighted-average common shares outstanding used to compute net loss per share, basic and diluted	31,663,243	8,546,741	8,374,674
Net loss per share, basic and diluted	$ (2.11)	$ (4.01)	$ (2.80)

Because we were in a net loss position for all periods presented, basic net loss per share is the same as diluted net loss per share for all periods, as the inclusion of all common stock equivalents outstanding would have been anti-dilutive. Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were, as of December 31, 2021, 2020, and 2019 as follows:

	As of December 31, 2021	As of December 31, 2020	As of December 31, 2019
Convertible preferred stock	—	14,119,631	14,119,631
Stock options outstanding	6,757,591	4,520,551	4,760,594
Shares committed under ESPP	18,804	—	—
Common shares subject to nonrecourse notes	—	409,795	409,795
	6,776,395	19,049,977	19,290,020

16. Unaudited Quarterly Results

The results of operations on a quarterly basis for the years ended December 31, 2021 and 2020 are set forth below:

	March 31, 2021	June 30, 2021	September 30, 2021	December 31, 2021
	(Amounts in thousands except per share data)			
License and collaboration revenue	$ 1,586	$ 1,476	$ 3,977	$ 2,559
Operating expenses:				
Research and development	10,165	11,146	15,833	15,111
General and administrative	4,596	5,113	6,760	7,853
Total operating expenses	14,761	16,259	22,593	22,964
Loss from operations	(13,175)	(14,783)	(18,616)	(20,405)
Total other income (expense)	16	472	(2,358)	2,247
Net loss before provision for (benefit from) income taxes	$ (13,159)	$ (14,311)	$ (20,974)	$ (18,158)
Provision for (benefit from) income taxes	—	—	—	321
Net loss	$ (13,159)	$ (14,311)	$ (20,974)	$ (18,479)
Net loss per share, basic and diluted	$ (1.39)	$ (1.39)	$ (0.46)	$ (0.31)
Weighted-average common shares outstanding, basic and diluted	9,499,448	10,261,770	45,889,646	60,180,759

	March 31, 2020	June 30, 2020	September 30, 2020	December 31, 2020
	(Amounts in thousands except per share data)			
License and collaboration revenue	$ 1,701	$ 8,478	$ 1,198	$ 984
Operating expenses:				
Research and development	8,641	7,580	6,180	12,024
General and administrative	3,489	3,153	3,247	4,171
Total operating expenses	12,130	10,733	9,427	16,195
Loss from operations	(10,429)	(2,255)	(8,229)	(15,211)
Interest income (expense)	(573)	333	83	154
Net loss before provision for (benefit from) income taxes	(11,002)	(1,922)	(8,146)	(15,057)
Provision for (benefit from) income taxes	(1,202)	(50)	(213)	(354)
Net loss	$ (9,800)	$ (1,872)	$ (7,933)	$ (14,703)
Net loss per share, basic and diluted	$ (1.16)	$ (0.22)	$ (0.93)	$ (1.68)
Weighted-average common shares outstanding, basic and diluted	8,429,410	8,441,934	8,537,965	8,775,242

17. Subsequent Events

We have entered into a new lease agreement with a commencement date of January 13, 2022, for an additional 10,000 square feet of laboratory and office space located in Berkeley, California. We have the option to extend the lease for five years. Our monthly base rent amounts to $0.1 million, subject to annual escalation of 3.5% with a total minimum lease payment of $9.2 million. The lease includes a tenant improvement allowance of up to $1.8 million.

Exhibit 4.1

CARIBOU BIOSCIENCES, INC.
DESCRIPTION OF COMMON STOCK

Caribou Biosciences, Inc. (the "Company") has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") – common stock, par value $0.0001 per share (the "Common Stock"). The Common Stock trades on The Nasdaq Global Select Market under the trading symbol "CRBU."

The following summary description sets forth some of the general terms and provisions of the Common Stock. Because this is a summary description, it does not contain all of the information that may be important to you. For a more detailed description of the Common Stock, you should refer to the Company's Amended and Restated Certificate of Incorporation (the "Certificate of Incorporation") and the Amended and Restated Bylaws (the "Bylaws"), which are filed as exhibits to the Annual Report on Form 10-K to which this description is filed as an exhibit.

The Company's authorized capital stock consists of 310,000,000 shares, all with a par value of $0.0001 per share, 300,000,000 of which are designated as Common Stock and 10,000,000 of which are designated as preferred stock.

Common Stock

Holders of the Company's common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders, except for certain votes that relate solely to the terms of preferred stock, and do not have cumulative voting rights in the election of directors. An election of directors by the Company's stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by the Company's board of directors, subject to any preferential dividend rights of any series of preferred stock that the Company may designate and issue in the future.

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of the Company's common stock are entitled to receive dividends as may be declared from time to time by the Company's board of directors out of legally available funds.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately the Company's net assets legally available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock will have no preemptive, subscription, redemption or conversion rights, and there are no redemption or sinking fund provisions applicable to the Company's common stock. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that the Company may designate and issue in the future.

Anti-Takeover Effects of the Certificate of Incorporation and Bylaws

The Company's Certificate of Incorporation and Bylaws contain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the Company's board of directors, but which may have the effect of delaying, deferring, or preventing a future takeover or change in control of the Company unless such takeover or change in control is approved by the Company's board of directors.

These provisions include:

Classified Board. The Certificate of Incorporation provides that, other than any directors elected by the separate vote of one or more series of preferred stock (if any) who are entitled to elect directors, the board of directors will be divided into three classes of directors. As a result, approximately one-third of the board of directors will be elected each year. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of the Company's board of directors. The Certificate of Incorporation also provides that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of

directors will be fixed exclusively pursuant to one or more resolutions adopted from time to time by the board of directors.

Action by Written Consent; Special Meetings of Stockholders. The Certificate of Incorporation provides that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent. The Certificate of Incorporation and Bylaws also provide that, except as otherwise required by statute and subject to the rights, if any, of the holders of any series of preferred stock, special meetings of the stockholders can only be called pursuant to a resolution adopted by a majority of the board of directors, the chair of the board of directors, or the Company's chief executive officer. Except as described above, stockholders will not be permitted to call a special meeting or to require the Company's board of directors to call a special meeting.

Removal of Directors. The Certificate of Incorporation provides that, subject to the special rights of the holders of one or more series of preferred stock (if any) to elect directors, directors may be removed only for cause by the affirmative vote of at least 66 2/3% of the voting power of the Company's outstanding shares of capital stock, voting together as a single class. This requirement of a supermajority vote to remove directors could enable a minority of the Company's stockholders to prevent a change in the composition of our board.

Advance Notice Procedures. The Bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting will only be able to consider proposals or nominations specified in the Company's notice of meeting or brought before the meeting specifically by or at the direction of the board of directors or by a stockholder who was a stockholder of record both at the time of giving the stockholder's notice referenced below and at the time of the meeting, who is entitled to vote at the meeting and is present in person at the meeting, and who has given the Secretary of the Company timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting and must update and supplement that written notice on a timely basis as described in the Bylaws. Although the Bylaws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the Bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the Company.

Supermajority Approval Requirements. The Delaware General Corporation Law ("DGCL") generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless either a corporation's certificate of incorporation or bylaws requires a greater percentage. The Certificate of Incorporation and Bylaws provide that the affirmative vote of holders of at least 66 2/3% of the voting power of all of the Company's then-outstanding shares of capital stock entitled to vote generally in the election of directors will be required to adopt, amend or repeal Bylaws and certain specified provisions of the Certificate of Incorporation. This requirement of a supermajority vote to approve amendments to the Certificate of Incorporation and Bylaws could enable a minority of the Company's stockholders to exercise veto power over any such amendments.

Authorized but Unissued Shares. The Company's authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital, corporate acquisitions, and employee benefit plans. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of the Company's common stock by means of a proxy contest, tender offer, merger, or otherwise.

Exclusive Forum. The Certificate of incorporation requires, to the fullest extent permitted by law, that derivative actions brought on behalf of the Company, actions against current or former directors, officers, employees, agents, or stockholders for breach of a fiduciary duty, and other similar actions may be brought only in specified courts in the State of Delaware. This exclusive forum provision explicitly does not apply to actions arising under federal securities laws, including suits brought to enforce any liability or duty created by the Securities Act of 1933, as amended (the "Securities Act"), the Exchange Act, or any other claim for which federal courts have exclusive jurisdiction. Furthermore, the Certificate of incorporation also provides that unless the Company consents in writing to the selection of an alternative forum, the federal district courts of the United States will be the exclusive

forum for the resolution of any compliant asserting a cause of action arising under the Securities Act. Although the Company believes these provisions benefit the Company by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, these provisions may have the effect of discouraging lawsuits against the Company's directors and executive officers.

Section 203 of the DGCL

The Company is 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. A "business combination" includes, among other things, a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock.

Under Section 203 of the DGCL, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: (i) before the stockholder became interested, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; (ii) 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; or (iii) at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation 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.

A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. The Company has not opted out of Section 203 of the DGCL. As a result, mergers or other takeover or change in control attempts of the Company may be discouraged or prevented.

Transfer Agent and Registrar

The transfer agent and registrar for the Company's common stock is Computershare Trust Company, N.A. The transfer agent and registrar's address is 150 Royall Street, Canton, Massachusetts 02021.

Exhibit 10.27

FIRST AMENDMENT
(2929 Seventh Street, Berkeley, California)

This First Amendment (this "**Amendment**"), dated as of January II, 2022, is entered into by and between 2929 SEVENTH ST., LLC, a California limited liability company ("**Landlord**"), and CARIBOU BIOSCIENCES, INC., a Delaware corporation ("**Tenant**").

Recitals

A. Landlord and Tenant entered into that certain Amended and Restated Office/Laboratory dated March 31, 202I (the "**Lease**"), whereby Tenant leases certain space known as Suites 100, 105, 110, and 120 and consisting of approximately 61,73 5 square feet of Rentable Area (the "**Premises**") within the building located at 2929 Seventh Street, Berkeley, California (the "**Building**").

B. Dated concurrently with this Amendment, Landlord's affiliate, 7th Street Property Ill General Partnership, a California general partnership, as landlord, and Tenant, have entered into that certain Office/Laboratory, whereby Tenant shall lease the entirety of the building located at 2895 Seventh Street, Berkeley, California, and consisting of approximately 10,000 square feet of Rentable Area (the "**2895 Seventh Street Premises**").

C. In order to accommodate Tenant's parking requirements at the 2895 Seventh Street Premises, but not overburden the parking available for all tenants of the Campus, Landlord and Tenant have agreed to reduce the parking spaces available for Tenant's use at the Building in order for Tenant to have such parking spaces available for its use at the 2895 Seventh Street Premises, on the following terms and conditions.

NOW THEREFORE, in consideration of the foregoing and the mutual covenants contained herein, the parties agree as follows:

Agreement

1. Definitions; Recitals. Unless otherwise specified herein, all capitalized terms used in this Amendment are used as defined in the Lease. The parties acknowledge the truthfulness of the foregoing Recitals, which are hereby incorporated into this Amendment.

2. Inconsistencies. To the extent that there are any inconsistencies between the terms of the Lease and this Amendment, the terms of this Amendment shall control.

3. Parking. Section 1.1(12) of the Lease is hereby deleted and replaced with the following:

(12) PARKING:

(a) Up to 83 parking spaces in the following parking areas:

Lot located on
East Side of Building (the "East Lot"):
44 spaces reserved for the exclusive use of Tenant (the "Building Spaces")

Parking structures located within the Campus
as shown on Exhibit A-2 hereto ("Aquatic Park Lot"):
39 unreserved spaces

(b) The rates for the parking spaces shall be as follows:

The Building Spaces (44 spaces): $0.00/space/month, through December 31, 2023; thereafter, commencing as of January 1, 2024, $61.00/space/month, through December 31, 2025; thereafter, commencing as of January 1, 2026, at the standard prevailing monthly rates being charged from time to time by Landlord or its parking operator without regard to discounts provided to any other occupants of the Building (the "Standard Parking Rates")

30 spaces: $61.00/space/month, through December 31, 2025; thereafter, commencing as of January 1, 2026, at the Standard Parking Rates

9 spaces: At the Standard Parking Rates. The current rate for unreserved parking spaces is $135.00/space/month.

(c) Use of 999/2919 Lot. Tenant shall be permitted to use the 999/2919 Lot (identified as "Area A" on Exhibit A-2 to this Lease) solely for use of the EV charging stations, and only when Tenant's employees' vehicles are actively charging (the "EV Charging Rights"). Landlord may revoke the EV Charging Rights at any time during the Term upon not less than thirty (30) days' prior written notice to Tenant.

4. Miscellaneous.

(a) This Amendment sets forth the entire agreement between the parties with respect to the matters set forth herein. There have been no additional oral or written representations or agreements. Under no circumstances shall Tenant be entitled to any Rent abatement, improvement allowance, leasehold improvements, or other work to the Premises, or any similar economic incentives that may have been provided Tenant in connection with entering into the Lease, unless specifically set forth in this Amendment.

(b) Except as herein modified or amended, the provisions, conditions and terms of the Lease shall remain unchanged and in full force and effect.

(c) In the case of any inconsistency between the provisions of the Lease and this Amendment, the provisions of this Amendment shall govern and control.

(d) Submission of this Amendment by Landlord is not an offer to enter into this Amendment but rather is a solicitation for such an offer by Tenant. Landlord shall not be bound by this Amendment until Landlord has executed and delivered the same to Tenant.

(e) The capitalized terms used in this Amendment shall have the same definitions as set forth in the Lease to the extent that such capitalized terms are defined therein and not redefined in this Amendment.

(f) This Amendment may be executed in counterparts each of which counterparts when taken together shall constitute one and the same agreement. Any facsimile, PDF or other electronic signature shall constitute a valid and binding method for executing this Amendment. Executed counterparts of this Amendment exchanged by facsimile transmission, PDF email, or other electronic means shall be fully enforceable.

IN WITNESS WHEREOF, the parties have executed this Amendment as of the date set forth above.

TENANT:

CARIBOU BIOSCIENCES, INC. ,
a Delaware corporation

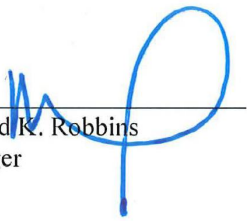
By: DocuSigned by: RoEH 9B8752B39BA2471...
Rachel E. Haurwitz, Ph.D.
its President and CEO

By: DocuSigned by: Barbara G. McClung 9A615A33279A4FA...
Barbara G. McClung, J.D.
its Chief Legal Officer and Secretary

LANDLORD:

2929 SEVENTH ST., LLC,
a California limited liability company

By: Wareham-NZL, LLC, its Manager

By: 
Name: Richard K. Robbins
Its: Manager

RIDER 1

COMMENCEMENT DATE AGREEMENT

Wareham-NZL, LLC, a California limited liability company ("Landlord"), and Caribou Biosciences, a Delaware Corporation ("Tenant"), have entered into a certain Office/Laboratory Lease dated as of January 11, 2022 (the "Lease").

WHEREAS, Landlord and Tenant wish to confirm and memorialize the Commencement Date of the Lease as provided for in Section 2.2 of the Lease;

NOW, THEREFORE, in consideration of the foregoing and the mutual covenants contained herein and in the Lease, Landlord and Tenant agree as follows:

1. Unless otherwise defined herein, all capitalized terms shall have the same meaning ascribed to them in the Lease.

2. The Commencement Date (as defined in the Lease) of the Lease is January 13, 2022.

3. Tenant hereby confirms the following:

(a) That it has accepted possession of the Premises pursuant to the terms of the Lease; and

(b) That the Lease is in full force and effect.

4. Except as expressly modified hereby, all terms and provisions of the Lease are hereby ratified and confirmed and shall remain in full force and effect and binding on the parties hereto.

5. The Lease and this Commencement Date Agreement contain all of the terms, covenants, conditions and agreements between Landlord and Tenant relating to the subject matter herein. No prior other agreements or understandings pertaining to such matters are valid or of any force and effect.

TENANT:

Caribou Biosciences, Inc.

a Delaware corporation

By: _____

Print Name: Rachel E. Haurwitz, Ph.D.

Its: President & CEO

By: _____

Print Name: Barbara G. McClung, J.D.

Its: Chief Legal Officer and Secretary

LANDLORD: 7th Street Property III General Partnership, a California general partnership

Wareham-NZL, LLC, its Manager, a California limited liability company, its Managing General Partner

By: _____

Richard K. Robbins

Managing Member

[INSERT CORRECT SIGNATURE BLOCK FOR PROPERTY]

Exhibit 10.31

February 11, 2022

Rachel E Haurwitz
XXXXXXXXX
XXXXXXXXX

Dear Rachel:

I am pleased to announce that the Caribou Board of Directors has approved a bonus based on the Company's achievements in 2021. You will receive a one-time payment of $319,069, less applicable withholding taxes, on February 22, 2022. Congratulations! Additionally, your base salary has been increased to $605,000, effective January 1, 2022. Your February 15, 2022 paycheck will reflect your new salary as well as a retroactive payment back to January 1 for your salary increase. Your target bonus will be 55% in 2022 for your role as President and CEO.

2021 was a pivotal year for the Company as we signed a license and collaboration agreement with AbbVie, closed the Series C financing, and became a publicly traded company. Additionally, as publicly disclosed in July, the first patient was dosed in Caribou's Phase 1 ANTLER clinical trial for our allogeneic anti-CD19 CAR-T cell therapy (CB-010). The other members of the Board and I are grateful to you for your hard work and your achievements in 2021. Caribou has the exciting and challenging opportunity to transform the field of medicine with our product candidates. Only through the continued collective efforts of the herd will we achieve our ambitious 2022 goals.

All other terms and conditions of your employment are governed by the Officer Employment Agreement between you and the Company, dated July 27, 2021. Thank you again for your contributions to the Company's accomplishments in 2021. Please let Cindy know if you wish to contribute to your 401(k) account from your bonus payment.

I am excited about all we will accomplish together in 2022!

Best regards,

/s/ Barbara G. McClung
Barbara G. McClung
Chief Legal Officer and Corporate Secretary

Exhibit 10.33

Confidential

January 5, 2021

Jason O'Byrne
XXXXXXXXX
XXXXXXXXX
XXXXXXXXX

RE: Offer of Employment with Caribou Biosciences, Inc.

Dear Jason:

On behalf of Caribou Biosciences, Inc. (the "Company" or "Caribou"), I am pleased to invite you to join the Company as Chief Financial Officer, reporting to Rachel E. Haurwitz, President and Chief Executive Officer. The first day of your employment will be February XX, 2021 or such other date as you and the Company mutually agree in writing.

The terms of this offer of employment are as follows:

1. Compensation. If you decide to join us, you will be paid an annual salary of $385,000.00 which will be paid twice a month in accordance with the Company's normal payroll procedures. As a Caribou employee, you will also be eligible to receive certain employee benefits. The details of these employee benefits are explained in the attached Description of Benefits. You are eligible for performance-based incentives after evaluation by the Caribou management team. Currently, the target bonus for your position is set at 35%. Evaluations are typically done on an annual basis. You should note that the Company may modify job titles, wages and benefits from time to time at its sole discretion.

The Company will pay you a one-time, contingency payment of $70,000.00, if the Company closes a Series C financing of at least $50 million, and payable only in the event that you do not receive a bonus for 2020 from your current employer. You will receive this payment within fifteen (15) calendar days after the Series C financing closes if you are an employee on that date, or with the next Company's payroll if you join the Company after that date. If you choose to leave the Company prior to one (1) year from the date of the contingency payment or your employment is terminated for cause prior to one (1) year from the date of the contingency payment, you will be responsible for repaying the Company the contingency payment subject to a reduction for each month of employment. (For example, if you leave the Company six (6) months after the date of the contingency payment, you will owe the Company $35,000.00.)

2. Stock Option Grant. In addition, if you decide to join the Company, it will be recommended to the Company's Board of Directors that the Company grant you an option to

purchase a number of shares of the Company's Common Stock representing one percent (1%) of the Company's total number of fully diluted shares on the date of the grant at a price per share equal to the fair market value per share of the Common Stock on the date of grant as determined by the Company's Board of Directors. Twenty-five percent (25%) of the shares subject to the option grant shall vest 12 months after the date your vesting begins subject to your continuing employment with the Company, and no shares shall vest before the one-year cliff. The remaining shares subject to the option grant shall vest monthly thereafter (1/48 of the grant per month for the 36 months following the one-year cliff) subject to your continuing employment with the Company. The stock option grant shall be subject to the terms and conditions of the Company's Equity Incentive Plan and Stock Option Agreement, including vesting requirements (the "Stock Agreements"). No right to any stock is earned or accrued until such time that vesting occurs, nor does the grant confer any right to continue vesting or employment. If the total number of fully diluted shares of Common Stock increases after the date of the grant due to the Company's Series C financing, you will receive an additional stock option grant so that your combined option grants to purchase a number of shares of the Company's Common Stock represent one percent (1%) of the Company's total number of fully diluted shares, subject to the same vesting schedule and at a price per share equal to the fair market value per share of the Common Stock on the date of grant as determined by the Company's Board of Directors.

3. Officer Employment Agreement. The Company is excited about your joining and looks forward to a beneficial and productive relationship. As an Officer of the Company, the terms and conditions of your employment will be as set forth in the enclosed Officer Employment Agreement to be executed by you and the Company. Additionally, your employment will be covered by an Indemnification Agreement.

4. Immigration. For purposes of federal immigration law, you will be required to provide to the Company documentary evidence of your identity and eligibility for employment in the United States. Such documentation must be provided to us within three (3) business days of your first day of employment with Caribou, or the Company may terminate your employment.

5. Prior Employment/Third Party Information. We also ask that, if you have not already done so, you disclose to the Company any and all agreements relating to your prior employment that may affect your eligibility to be employed by the Company or limit the manner in which you may be employed. It is the Company's understanding that any such agreements will not prevent you from performing the duties of your position and you represent that such is the case. Moreover, you agree that, during the term of your employment with the Company, you will not engage in any other employment, occupation, consulting or other business activity directly related to the business in which the Company is now involved or becomes involved during the term of your employment, nor will you engage in any other activities that conflict with your obligations to the Company. Similarly, you agree not to bring any third party confidential information to the Company, including that of your former employer, and that in performing your duties for the Company you will not in any way utilize any such information.

6. Company Rules and Policies. As a Company employee, you will be expected to abide by the Company's rules and policies and to acknowledge receipt of the same.

7. Confidential Information and Invention Assignment Agreement. As a condition of your employment, you are also required to sign and comply with a Confidential Information and Invention Assignment Agreement ("Confidentiality Agreement"), which requires, among other provisions, the assignment of patent rights to any invention made during your employment at the Company and non-disclosure of Company confidential information. A copy of the Confidentiality Agreement is attached hereto. Please note that we must receive your signed Confidentiality Agreement on or before the first day of your employment with the Company.

8. General. This Offer Letter together with the Officer Employee Agreement, Confidentiality Agreement, Indemnification Agreement, and Stock Agreements (if the above-referenced stock option grant is approved by the Board), when signed by you, set forth the terms of your employment with the Company and supersede any and all prior representations and agreements including, but not limited to, any representations made during your recruitment, interviews or pre-employment negotiations, whether written or oral. Any amendment of this Offer Letter or any waiver of a right under this Offer Letter must be in a writing signed by you and an officer of the Company. California law will govern this Offer Letter.

In the event of a conflict between the terms and provisions of this Offer Letter and the Officer Employee Agreement, Confidentiality Agreement, and/or Stock Agreements, the terms and provisions of the Officer Employee Agreement will control.

9. Confidential Offer of Employment. Until you have accepted this offer of employment, the terms of this offer (including compensation) should only be disclosed and discussed with your significant other, attorney, accountant, and/or tax advisor.

To accept the Company's offer of employment, please sign and date this letter in the space provided below. This offer of employment will terminate if the Offer Letter is not accepted, signed and returned by you to the Company on or before January 8, 2021. We look forward to your favorable reply and to working with you at Caribou Biosciences, Inc.

Sincerely,

/s/ Rachel E. Haurwitz

Rachel E. Haurwitz, Ph.D.
President and CEO

AGREED TO AND ACCEPTED:

Signature: /s/ Jason V. O'Byrne

Printed Name: Jason O'Byrne

Date: 1/06/2021

Enclosures:

Officer Employment Agreement
Indemnification Agreement
Confidential Information and Invention Assignment Agreement
Description of Benefits

Exhibit 10.34

February 11, 2022

Jason O'Byrne
XXXXXXXXX
XXXXXXXXX

Dear Jason:

I am pleased to announce that the Caribou Board of Directors has approved a bonus based on the Company's achievements in 2021. You will receive a one-time payment of $157,775, less applicable withholding taxes, on February 22, 2022. Congratulations! Additionally, your base salary has been increased to $440,000, effective January 1, 2022. Your February 15, 2022 paycheck will reflect your new salary as well as a retroactive payment back to January 1 for your salary increase. Your target bonus will be 40% in 2022 for your role as Chief Financial Officer. Your current manager is Rachel Haurwitz.

2021 was a pivotal year for the Company as we signed a license and collaboration agreement with AbbVie, closed the Series C financing, and became a publicly traded company. Additionally, as publicly disclosed in July, the first patient was dosed in Caribou's Phase 1 ANTLER clinical trial for our allogeneic anti-CD19 CAR-T cell therapy (CB-010). The other members of the Board and I are grateful to you for your hard work and your achievements in 2021. Caribou has the exciting and challenging opportunity to transform the field of medicine with our product candidates. Only through the continued collective efforts of the herd will we achieve our ambitious 2022 goals.

All other terms and conditions of your employment are governed by the Officer Employment Agreement between you and the Company, dated July 27, 2021. Thank you again for your contributions to the Company's accomplishments in 2021. Please let Cindy know if you wish to contribute to your 401(k) account from your bonus payment.

I am excited about all we will accomplish together in 2022!

Best regards,

/s/ Rachel E. Haurwitz

Rachel E. Haurwitz, Ph.D.
President and CEO

Exhibit 10.36

February 11, 2022

Barbara McClung
XXXXXXXXX
XXXXXXXXX

Dear Barbara:

I am pleased to announce that the Caribou Board of Directors has approved a bonus based on the Company's achievements in 2021. You will receive a one-time payment of $182,350 less applicable withholding taxes, on February 22, 2022. Congratulations! Additionally, your base salary has been increased to $455,000, effective January 1, 2022. Your February 15, 2022 paycheck will reflect your new salary as well as a retroactive payment back to January 1 for your salary increase. Your target bonus will be 40% in 2022 for your role as Chief Legal Officer. Your current manager is Rachel Haurwitz.

2021 was a pivotal year for the Company as we signed a license and collaboration agreement with AbbVie, closed the Series C financing, and became a publicly traded company. Additionally, as publicly disclosed in July, the first patient was dosed in Caribou's Phase 1 ANTLER clinical trial for our allogeneic anti-CD19 CAR-T cell therapy (CB-010). The other members of the Board and I are grateful to you for your hard work and your achievements in 2021. Caribou has the exciting and challenging opportunity to transform the field of medicine with our product candidates. Only through the continued collective efforts of the herd will we achieve our ambitious 2022 goals.

All other terms and conditions of your employment are governed by the Officer Employment Agreement between you and the Company, dated July 27, 2021. Thank you again for your contributions to the Company's accomplishments in 2021. Please let Cindy know if you wish to contribute to your 401(k) account from your bonus payment.

I am excited about all we will accomplish together in 2022!

Best regards,

/s/ Rachel E. Haurwitz
Rachel E. Haurwitz, Ph.D.
President and CEO

Exhibit 10.38

February 11, 2022

Steve Kanner
XXXXXXXXX
XXXXXXXXX

Dear Steve:

I am pleased to announce that the Caribou Board of Directors has approved a bonus based on the Company's achievements in 2021. You will receive a one-time payment of $181,100, less applicable withholding taxes, on February 22, 2022. Congratulations! Additionally, your base salary has been increased to $455,000, effective January 1, 2022. Your February 15, 2022 paycheck will reflect your new salary as well as a retroactive payment back to January 1 for your salary increase. Your target bonus will be 40% in 2022 for your role as Chief Scientific Officer. Your current manager is Rachel Haurwitz.

2021 was a pivotal year for the Company as we signed a license and collaboration agreement with AbbVie, closed the Series C financing, and became a publicly traded company. Additionally, as publicly disclosed in July, the first patient was dosed in Caribou's Phase 1 ANTLER clinical trial for our allogeneic anti-CD19 CAR-T cell therapy (CB-010). The other members of the Board and I are grateful to you for your hard work and your achievements in 2021. Caribou has the exciting and challenging opportunity to transform the field of medicine with our product candidates. Only through the continued collective efforts of the herd will we achieve our ambitious 2022 goals.

All other terms and conditions of your employment are governed by the Officer Employment Agreement between you and the Company, dated July 27, 2021. Thank you again for your contributions to the Company's accomplishments in 2021. Please let Cindy know if you wish to contribute to your 401(k) account from your bonus payment.

I am excited about all we will accomplish together in 2022!

Best regards,

/s/ Rachel E. Haurwitz
Rachel E. Haurwitz, Ph.D.
President and CEO

Exhibit 10.39

OFFICER EMPLOYMENT AGREEMENT

This Officer Employment Agreement ("Agreement") is dated as of November 8, 2021 ("Effective Date"), and is by and between Caribou Biosciences, Inc., a Delaware corporation, having an address at 2929 7th Street, Suite 105, Berkeley, CA 94710 (the "Company"), and Ruhi Khan, M.B.A. (the "Officer").

WHEREAS, the Company desires to employ the Officer and the Officer desires to be employed by the Company on the terms and conditions contained herein.

NOW, THEREFORE, in consideration of the mutual covenants and agreements herein contained and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties agree as follows:

1.Employment.

a. Term. The term of this Agreement shall commence on the Effective Date and continue until terminated in accordance with the provisions hereof (the "Term").

b. Position and Duties. During the Term, the Officer shall serve as Chief Business Officer of the Company and shall have supervision and control over and responsibility for the day-to-day business and affairs of the Company as may from time to time be prescribed by the Company's President and Chief Executive Officer, provided that such duties are consistent with the Officer' s position or other positions that they may hold from time to time. The Officer shall devote substantially all of their full working time and efforts to the business of the Company. Notwithstanding the foregoing, the Officer may serve on other boards of directors, with the approval of the Board, or sit on the governing boards of, or hold leadership positions related to community, charitable, academic, and religious activities, as long as such services and activities are disclosed to the Board and do not materially interfere with the Officer' s performance of their duties to the Company as provided in this Agreement.

2.Compensation and Related Matters.

a. Base Salary. During the Term, the Officer's initial annual base salary shall be $410,000.00. The Officer's base salary shall be reviewed from time to time by the Company's Board of Directors ("Board") or the Compensation Committee of the Board. The base salary in effect at any given time is referred to herein as "Base Salary." The Base Salary shall be payable in a manner that is consistent with the Company's usual payroll practices.

b. Incentive Compensation. During the Term, the Officer shall be eligible to receive cash incentive compensation as determined by the Board or the Compensation Committee from time to time. The Officer's initial target annual incentive compensation shall be 40% of their Base Salary. Except as otherwise provided herein, to earn incentive compensation, the Officer must be employed by the Company on the day such incentive compensation is paid.

c. Company Benefits. The Officer shall be entitled to all benefits received by employees of the Company in accordance with the Company's policies and plans.

3.Termination. During the Term, the Officer's employment hereunder may be terminated without any breach of this Agreement under the following circumstances:

a. Termination by the Company for Cause. The Company may terminate the Officer's employment hereunder for Cause. For purposes of this Agreement, "Cause" shall mean: (i) conduct by the Officer constituting a material act of misconduct in connection with the performance of their duties, including, without limitation, misappropriation of funds or property of the Company or any of its subsidiaries or affiliates other than the occasional, customary, and de minimis use of Company property for personal purposes; (ii) the commission by the

Officer of any felony or a misdemeanor involving moral turpitude, deceit, dishonesty or fraud, or any conduct by the Officer that would reasonably be expected to result in material injury or reputational harm to the Company or any of its subsidiaries and affiliates if they were retained in their position; (iii) continued non-performance by the Officer of their duties hereunder (other than by reason of the Officer's physical or mental illness, incapacity or disability) that has continued for more than 30. days following written notice of such non-performance from the Board; (iv) a material violation by the Officer of the Company's written policies; or (v) failure to cooperate with a bona fide internal investigation or an investigation by regulatory or law enforcement authorities, after being instructed by the Company to cooperate, or the willful destruction or failure to preserve documents or other materials known to be relevant to such investigation or the inducement of others to fail to cooperate or to produce documents or other materials in connection with such investigation.

b. Termination by the Company Without Cause. The Company may terminate the Officer's employment hereunder at any time without Cause upon written notice of such termination ("Notice of Termination"). Any termination by the Company of the Officer's employment under this Agreement which does not constitute a termination for Cause under Section 3(a) and does not result from the death or disability of the Officer under Section 3(d) or (e), respectively, shall be deemed a termination without Cause.

c. Termination by the Officer. The Officer may terminate their employment hereunder at any time for any reason, including but not limited to Good Reason. For purposes of this Agreement, "Good Reason" shall mean that the Officer has complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following events: (i) a material diminution in the Officer's responsibilities, authority or duties; (ii) the assignment of duties to the Officer that are materially inconsistent with their position; (iii) a decrease of more than 10% of the Officer's Base Salary except for across-the-board salary reductions based on the Company's financial performance similarly affecting all officers of the Company; (iv) a change by the Company in the Company location at which the Officer performs their duties to a location that is more than 50 miles (driving distance) from the original location; or (v) the material breach of this Agreement by the Company. "Good Reason Process" shall mean that (i) the Officer reasonably determines in good faith that a "Good Reason" condition has occurred; (ii) the Officer notifies the Company in writing of the first occurrence of the Good Reason condition within 30 days of the first occurrence of such condition; (iii) the Officer cooperates in good faith with the Company's efforts, for a period of 30 days following such notice (the "Cure Period"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) the Officer terminates their employment within 30 days after the end of the Cure Period. If the Company cures the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred.

d. Death. The Officer's employment hereunder shall terminate upon their death.

e. Disability. The Company may terminate the Officer's employment if they are disabled and unable to perform the essential functions of the Officer's then existing position or positions under this Agreement with or without reasonable accommodation for a period of 180 days (which need not be consecutive) in any 12-month period and the Company shall provide a Notice of Termination at that time. If any question shall arise as to whether during any period the Officer is disabled so as to be unable to perform the essential functions of the Officer's then existing position or positions with or without reasonable accommodation, the Officer may, and at the request of the Company shall, submit to the Company a certification in reasonable detail by a physician selected by the Company to whom the Officer or the Officer's guardian has no reasonable objection as to whether the Officer is so disabled or how long such disability is expected to continue, and such certification shall for the purposes of this Agreement be conclusive of the issue. The Officer shall cooperate with any reasonable request of the physician in connection with such certification. If such question shall arise and the Officer shall fail to submit such certification, the Company's determination of such issue shall be binding on the Officer. Nothing in this Section 3(b) shall be construed to waive the Officer's rights, if any, under existing federal and state law including, without limitation, the Family and Medical Leave Act of 1993,29 U.S.C. §2601, et seq. and the Americans with Disabilities Act, 42 U.S.C. §12101, et seq.

f. Notice of Termination. Except for termination as specified in Section 3(d), any termination of the Officer's employment by the Company or any such termination by the Officer shall be communicated by written Notice of Termination to the other party hereto. For purposes of this Agreement, a "Notice of Termination" shall mean a written notice which shall indicate the specific termination provision in this Agreement relied upon.

g. Date of Termination. "Date of Termination" shall mean: (i) if the Officer's employment is terminated by the Company for Cause under Section 3(a) or without Cause under Section 3(b) or on account of disability under Section 3(e), the date on which Notice of Termination is given; (ii) if the Officer's employment is terminated by the Officer under Section 3(c) without Good Reason, 30 days after the date on which a Notice of Termination is given; (iii) if the Officer's employment is terminated by the Officer under Section 3(c) with Good Reason, the date on which a Notice of Termination is given after the end of the Cure Period; and (iv) if the Officer's employment is terminated by their death, the date of their death. Notwithstanding the foregoing, in the event that the Officer gives a Notice of Termination to the Company under Section 3(c), the Company may unilaterally and solely at its own discretion accelerate the Date of Termination and such acceleration shall not result in a termination by the Company for purposes of this Agreement; provided, however, that in no event shall such accelerated Date of Termination be earlier than the date on which the Notice of Termination is delivered to the Company.

4.Compensation Upon Termination.

a. Termination Generally. If the Officer's employment with the Company is terminated for any reason, the Company shall pay or provide to the Officer (or to their authorized representative or estate) (i) any Base Salary earned through the Date of Termination, unpaid expense reimbursements in accordance with Company policy, and unused vacation that accrued through the Date of Termination on or before the time required by law but in no event more than 30 days after the Officer's Date of Termination; and (ii) any vested benefits the Officer may have under any employee benefit plan of the Company through the Date of Termination, which vested benefits shall be paid and/or provided in accordance with the terms of such employee benefit plans (collectively, the "Accrued Benefit").

b. Termination by the Company Without Cause or by the Officer with Good Reason. During the Term, if the Officer's employment is terminated by the Company without Cause as provided in Section 3(b), or the Officer terminates their employment for Good Reason as provided in Section 3(c), then the Company shall provide the Officer with the Accrued Benefit and the compensation and benefits set forth in this Section 4(b), the latter subject to the Officer signing a separation agreement containing, among other provisions, a general release of claims in favor of the Company and related persons and entities, confidentiality, return of property, and non-disparagement, in a form and manner satisfactory to the Company (the "Separation Agreement and Release") and the Separation Agreement and Release becoming fully effective, all within the time frame set forth in the Separation Agreement and Release: (i) the Company shall pay the Officer an amount equal to 9 months of the Officer's Base Salary (the "Severance Amount"); (ii) if the Officer (and their dependents, if applicable) was participating in the Company's group health plans immediately prior to the Date of Termination and the Officer elects COBRA health continuation for their self (and their dependents, if applicable), then the Company shall pay for 9 months or the Officer's COBRA health continuation period, whichever ends earlier, the COBRA health contribution that the Company would have made to provide health insurance to the Officer (and their dependents, if applicable) if the Officer had remained employed by the Company; provided, however, that the Company shall only be required to pay that percentage of dependent health insurance that the Company would be paying if the Officer had remained employed by the Company; and (iii) the amounts payable under Sections 4(b)(i) and (ii) shall be paid out in substantially equal installments in accordance with the Company's payroll practice over 9 months commencing on the first regularly scheduled payroll date that is at least 30 days after the Date of Termination, provided that the Separation Agreement and Release becomes fully effective; provided, however, that the initial payment shall include a catch-up payment to cover amounts retroactive to the day immediately following the Date of Termination. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2).

c. Change in Control. During the Term, if within 12 months after a Change in Control as defined herein, or within three months prior to a 409A Change in Control as defined herein, the Officer's employment is terminated by the Company without Cause as provided in Section 3(b) or the Officer terminates their employment for Good Reason as provided in Section 3(c), then, subject to the signing of the Separation Agreement and Release by the Officer and the Separation Agreement and Release becoming fully effective all within the time frame set forth in the Separation Agreement and Release, the Officer shall receive the benefits set forth in Section 4(b)(i) and (ii), and 100% of the Officer's then unvested stock options and time-based restricted stock shall become immediately vested; provided, however, that the number of months of base salary and benefits continuation in Sections 4(b)(i) and (ii) shall be increased to 12 months and the Officer shall also be provided with one times their target bonus amount for the year in which the Date of Termination occurs, which target bonus amount is payable in a lump sum on the first regularly scheduled payroll date that is at least 30 days following the Date of Termination or, if the Officer's employment was terminated within three months prior to a 409A Change in Control, upon the 409A Change in Control; provided, further that notwithstanding the language in Section 4(b)(iii), if the Change in Control is a change in the ownership or effective control of the Company, or in the ownership of a substantial portion of the Company's assets under Section 409A of the Code (a "409A Change in Control"), then the Severance Amount set forth in Section 4(b)(i) shall be payable as a lump sum on the first regularly scheduled payroll date that is at least 30 days following the Date of Termination, subject to the Separation Agreement and Release having become fully effective (for clarity, the COBRA payments set forth in Section 4(b)(ii) shall be paid in accordance with Section 4(b)(iii)) or, if the Officer's employment was terminated within three months prior to a 409A Change in Control, upon the 409A Change in Control. For purposes of this Section 4(c), "Change in Control" shall mean any of the following: (i) any "person," as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended (the "Act") (other than the Company, any of its subsidiaries, or any trustee, fiduciary or other person or entity holding securities under any employee benefit plan or trust of the Company or any of its subsidiaries), together with all "affiliates" and "associates" (as such terms are defined in Rule 12b-2 under the Act) of such person, shall become the "beneficial owner" (as such term is defined in Rule 13d-3 under the Act), directly or indirectly, of securities of the Company representing 50% or more of the combined voting power of the Company's then outstanding securities having the right to vote in an election of the Board ("Voting Securities") (in such case other than as a result of an acquisition of securities directly from the Company); or (ii) the date a majority of the members of the Board is replaced during any 12-month period by directors whose appointment or election is not endorsed by a majority of the members of the Board before the date of the appointment or election; or (iii) the consummation of (A) any consolidation or merger of the Company where the stockholders of the Company, immediately prior to the consolidation or merger, would not, immediately after the consolidation or merger, beneficially own (as such term is defined in Rule 13d-3 under the Act), directly or indirectly, shares representing in the aggregate more than 50% of the voting shares of the Company issuing cash or securities in the consolidation or merger (or of its ultimate parent corporation, if any), or (B) any sale or other transfer (in one transaction or a series of transactions contemplated or arranged by any party as a single plan) of all or substantially all of the assets of the Company. Notwithstanding the foregoing, a "Change in Control" shall not be deemed to have occurred for purposes of the foregoing clause solely as the result of an acquisition of securities by the Company that, by reducing the number of shares of Voting Securities outstanding, increases the proportionate number of Voting Securities beneficially owned by any person to 50% or more of the combined voting power of all of the then outstanding Voting Securities; provided, however, that if any person referred to in this sentence shall thereafter become the beneficial owner of any additional shares of Voting Securities (other than pursuant to a stock split, stock dividend, or similar transaction or as a result of an acquisition of securities directly from the Company) and immediately thereafter beneficially owns 50% or more of the combined voting power of all of the then outstanding Voting Securities, then a "Change in Control" shall be deemed to have occurred.

5. Additional Limitations and Section 409A.

a. Additional Limitations. Notwithstanding anything to the contrary in this Agreement, in the event that the amount of any compensation, payment or distribution by the Company to or for the benefit of the Officer, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a

manner consistent with Section 280G of the Internal Revenue Code of 1986, as amended (the "Code"), and the applicable regulations thereunder (the "Aggregate Payments"), would be subject to the excise tax imposed by Section 4999 of the Code, then the Aggregate Payments shall be reduced (but not below zero) so that the sum of all of the Aggregate Payments shall be $1.00 less than the amount at which the Officer becomes subject to the excise tax imposed by Section 4999 of the Code; provided that such reduction shall only occur if it would result in the Officer receiving a higher After Tax Amount (as defined below) than the Officer would receive if the Aggregate Payments were not subject to such reduction. In such event, the Aggregate Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Aggregate Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 280G of the Code: (1) cash payments not subject to Section 409A of the Code; (2) cash payments subject to Section 409A of the Code; (3) equity-based payments and acceleration; and (4) non-cash forms of benefits; provided that in the case of all the foregoing Aggregate Payments all amounts or payments that are not subject to calculation under Treas. Reg. § 1.280G-1, Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. § 1.280G-1, Q&A-24(b) or (c). For purposes of this Section 5(a), the "After Tax Amount" means the amount of the Aggregate Payments less all federal, state, and local income, excise and employment taxes imposed on the Officer as a result of the Officer's receipt of the Aggregate Payments. For purposes of determining the After Tax Amount, the Officer shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes. The determination as to whether a reduction in the Aggregate Payments shall be made pursuant to Section 5(b)(i) shall be made by a nationally recognized accounting firm selected by the Company (the "Accounting Firm"), which shall provide detailed supporting calculations both to the Company and the Officer within 15 business days of the Date of Termination, if applicable, or at such earlier time as is reasonably requested by the Company or the Officer. Any determination by the Accounting Firm shall be binding upon the Company and the Officer.

b. Section 409A. Notwithstanding anything to the contrary in this Agreement, if at the time of the Officer's separation from service within the meaning of Section 409A of the Code, the Company determines that the Officer is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that the Officer becomes entitled to under this Agreement on account of the Officer's separation from service would be considered deferred compensation otherwise subject to the 20% additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) 6 months and one day after the Officer's separation from service or (B) the Officer's death. If any such delayed cash payment is otherwise payable on an installment basis, the first payment shall include a catch-up payment covering amounts that would otherwise have been paid during the six-month period but for the application of this provision, and the balance of the installments shall be payable in accordance with their original schedule. All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by the Officer during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year (except for any lifetime or other aggregate limitation applicable to medical expenses). Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit. To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon the Officer's termination of employment, then such payments or benefits shall be payable only upon the Officer's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-l(h). The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code,

the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party. The Company makes no representation or warranty and shall have no liability to the Officer or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section 409A.

6.Litigation and Regulatory Cooperation. During and after the Term, the Officer shall cooperate fully with the Company in the defense or prosecution of any claims or actions now in existence or which may be brought in the future against or on behalf of the Company that relate to events or occurrences that transpired while the Officer was employed by the Company. The Officer's full cooperation in connection with such claims or actions shall include, but not be limited to, being available to meet with counsel to prepare for discovery or trial and to act as a witness on behalf of the Company at mutually convenient times. During and after the Term, the Officer also shall cooperate fully with the Company in connection with any investigation or review of any federal, state or local regulatory authority as any such investigation or review relates to events or occurrences that transpired while the Officer was employed by the Company. The Company shall reimburse the Officer for any reasonable out-of-pocket expenses incurred in connection with the Officer's performance of obligations pursuant to this Section 6 and, after their employment with the Company terminates, the Officer may be entitled for reasonable compensation for their time. For the avoidance of doubt, nothing in this Agreement shall be interpreted or applied to prohibit the Officer from making any good faith report to any governmental agency or other governmental entity concerning any act or omission that the Officer reasonably believes constitutes a possible violation of federal or state law or making other disclosures that are protected under the anti-retaliation or whistleblower provisions of applicable federal or state law or regulation.

7.Relief. The Officer agrees that it would be difficult to measure any damages caused to the Company which might result from any breach by the Officer of this Agreement, and that in any event money damages would be an inadequate remedy for any such breach. Accordingly, the Officer agrees that if the Officer breaches, or proposes to breach, this Agreement, the Company shall be entitled, in addition to all other remedies that it may have, to an injunction or other appropriate equitable relief to restrain any such breach without showing or proving any actual damage to the Company. In addition, in the event the Officer breaches the Confidential Information and Invention Assignment Agreement, effective as of November 8, 2021, by and between the Company and the Officer ("CIIA"), during a period when they are receiving severance payments pursuant to Section 4(b) or (c), the Company shall have the right to suspend or terminate such severance payments. Such suspension or termination shall not limit the Company's other options with respect to relief for such breach and shall not relieve the Officer of their duties under this Agreement.

8.Governing Law and Jurisdiction. This Agreement shall be governed by the laws of the State of California, and the parties hereby consent to the jurisdiction of the state and federal courts in the State of California.

9.Integration. This Agreement constitutes the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior agreements between the parties concerning such subject matter, with the sole exception of the CIIA and the Indemnification Agreement, dated November 8, 2021, both by and between the Company and the Officer. If there are any conflicts between the terms and conditions of the CIIA and this Agreement, the terms and conditions of this Agreement shall govern.

10.Successor to the Officer. This Agreement shall inure to the benefit of and be enforceable by the Officer's personal representatives, executors, administrators, heirs, distributees, devisees and legatees. In the event of the Officer's death after their termination of employment but prior to the completion by the Company of all payments due them under this Agreement, the Company shall continue such payments to the Officer's beneficiary designated in writing to the Company prior to their death (or to their estate, if the Officer fails to make such designation).

11.Enforceability. If any portion or provision of this Agreement (including, without limitation, any portion or provision of any section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of

competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

12.Survival. The provisions of this Agreement shall survive the termination of this Agreement and/or the termination of the Officer's employment to the extent necessary to effectuate the terms contained herein.

13.Waiver. No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement, or the waiver by any party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

14.Notices. Any notices, requests, demands and other communications provided for by this Agreement shall be sufficient if in writing and delivered in person or sent by a nationally recognized overnight courier service or by registered or certified mail, postage prepaid, return receipt requested, to the Officer at the last address the Officer has filed in writing with the Company or, in the case of the Company, at the address set forth above to the President and Chief Executive Officer with a copy to legalnotices@cariboubio.com; provided that if the Officer providing notice is the President and Chief Executive Officer, they are not required to provide notice to themself but instead shall provide written notice to the Chief Legal Officer.

15.Amendment. This Agreement may be amended or modified only by a written instrument signed by the Officer and by a duly authorized representative of the Company.

16.Successor to Company. The Company shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business or assets of the Company expressly to assume and agree to perform this Agreement to the same extent that the Company would be required to perform it if no succession had taken place. Failure of the Company to obtain an assumption of this Agreement at or prior to the effectiveness of any succession shall be a material breach of this Agreement.

17.Counterparts. This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original; but such counterparts shall together constitute one and the same document.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the Effective Date.

Caribou Biosciences, Inc.

By: 
Name: Rachel E. Haurwitz, Ph.D.
Title: President and CEO

Ruhi Khan, M.B.A.

By: 
Ruhi Khan

Exhibit 10.40

February 11, 2022

Ruhi Khan
311 Cervantes Road
Portola Valley, CA 94028

Dear Ruhi:

I am pleased to announce that the Caribou Board of Directors has approved a bonus based on the Company's achievements in 2021. You will receive a one-time payment of $26,650, less applicable withholding taxes, on February 22, 2022. Congratulations! Your base salary is $410,000 and your target bonus will be 40% in 2022 for your role as Chief Business Officer. Your current manager is Rachel Haurwitz.

2021 was a pivotal year for the Company as we signed a license and collaboration agreement with AbbVie, closed the Series C financing, and became a publicly traded company. Additionally, as publicly disclosed in July, the first patient was dosed in Caribou's Phase 1 ANTLER clinical trial for our allogeneic anti-CD19 CAR-T cell therapy (CB-010). The other members of the Board and I are grateful to you for your hard work and your achievements in 2021. Caribou has the exciting and challenging opportunity to transform the field of medicine with our product candidates. Only through the continued collective efforts of the herd will we achieve our ambitious 2022 goals.

All other terms and conditions of your employment are governed by the Officer Employment Agreement between you and the Company, dated November 8, 2021. Thank you again for your contributions to the Company's accomplishments in 2021. Please let Cindy know if you wish to contribute to your 401(k) account from your bonus payment.

I am excited about all we will accomplish together in 2022!

Best regards,

/s/ Rachel E. Haurwitz

Rachel E. Haurwitz, Ph.D.
President and CEO
Caribou Biosciences, Inc., 2929 7th Street, Suite 105, Berkeley, CA 94710; (510) 982-6030

Exhibit 10.41

Confidential

October 29, 2021

Syed Rizvi, M.D.
XXXXXXXXX
XXXXXXXXX
XXXXXXXXX

RE: Offer of Employment with Caribou Biosciences, Inc.

Dear Syed:

On behalf of Caribou Biosciences, Inc. (the "Company" or "Caribou"), I am pleased to invite you to join the Company as Chief Medical Officer, reporting to Rachel E. Haurwitz, President and Chief Executive Officer. The first day of your employment will be January 18, 2022, or such other date as you and the Company mutually agree in writing.

The terms of this offer of employment are as follows:

1. Compensation. If you decide to join us, you will be paid an annual salary of $490,000.00, which will be paid twice a month in accordance with the Company's normal payroll procedures. As a Caribou employee, you will also be eligible to receive certain employee benefits. The details of these employee benefits are explained in the attached Description of Benefits. You are eligible for performance-based incentives after evaluation by the Caribou management team. Currently, the target bonus for your position is set at 40%. Evaluations are typically done on an annual basis. You should note that the Company may modify job titles, wages, and benefits from time to time at its sole discretion.

The Company will pay you a one-time, sign-on bonus in the amount of $150,000.00, which will be paid through payroll upon the Company's completion of an acceptable background check. If you choose to leave the Company prior to one (1) year from your first day of employment with the Company or your employment is terminated for cause prior to the first year of employment, you will be responsible for repaying the Company this sign-on bonus; provided, however, this amount will be reduced on a monthly basis over the year. (For example, if you leave the Company six (6) months after your first day of employment, you will owe the Company $75,000.00.)

2. Stock Option and Restricted Stock Units Grants. In addition, the Company will grant you an option to purchase 161,250 shares of the Company's Common Stock (the "Option") on the date that is five (5) trading days after your first day of employment with

the Company (the "Grant Date"). The exercise price per share of the Option will be equal to the market value per share of the Common Stock on the Grant Date. Twenty-five percent (25%) of the Option shares will vest 12 months after your first day of employment subject to your continuing employment with the Company, and no shares will vest before the one-year date. The remaining Option shares will vest monthly thereafter (1/48 of the grant per month for the 36 months following the one-year cliff) subject to your continuing employment with the Company. The Option will be subject to the terms and conditions of the Company's 2021 Equity Incentive Plan and Stock Option Agreement, including vesting requirements (the "Stock Agreements"). No right to any stock is earned or accrued until such time that vesting occurs, nor does the grant confer any right to continue vesting or employment.

The Company will also grant you 60,000 Restricted Stock Units ("RSUs") of the Company's Common Stock on the date that is five (5) trading days after your first day of employment with the Company (the "Grant Date"). Twenty-five percent (25%) of the RSUs will vest on first anniversary of your first day of employment and twenty-five percent (25%) will vest on each of the next three (3) successive anniversaries subject to your continuing employment with the Company. The RSUs will be subject to the terms and conditions of the Company's 2021 Equity Incentive Plan. Annual vesting of the RSUs will be a taxable event and you will be responsible to satisfy the applicable tax obligations associated therewith. No right to any stock is earned or accrued until such time that vesting occurs, nor does the grant confer any right to continue vesting or employment.

3. Officer Employment Agreement and Indemnification Agreement. As an executive officer of the Company, the Company will enter into an Officer Employment Agreement and an Indemnification Agreement (collectively, "Officer Agreements"). Copies of each are attached hereto. The Officer Agreements will be executed on your first day of employment with the Company.

4. Immigration. For purposes of federal immigration law, you will be required to provide to the Company documentary evidence of your identity and eligibility for employment in the United States. Such documentation must be provided to us within three (3) business days of your first day of employment with the Company, or the Company may terminate your employment.

5. Prior Employment/Third Party Information. We also ask that, if you have not already done so, you disclose to the Company any and all agreements relating to your prior employment that may affect your eligibility to be employed by the Company or limit the manner in which you may be employed. It is the Company's understanding that any such agreements will not prevent you from performing the duties of your position and you represent that such is the case. Moreover, you agree that, during the term of your employment with the Company, you will not engage in any other employment, occupation, consulting, or other business activity directly related to the business in which the Company is now involved or becomes involved during the term of your employment, nor will you engage in any other activities that conflict with your obligations to the Company. Similarly, you agree not to bring any third party confidential information to the Company, including

that of your former employer, and that in performing your duties for the Company you will not in any way utilize any such information.

6. Company Rules and Policies. As a Company employee, you will be expected to abide by the Company's rules and policies and to acknowledge receipt of the same.

7. Confidential Information and Invention Assignment Agreement. As a condition of your employment, you are also required to sign and comply with a Confidential Information and Invention Assignment Agreement ("CIIAA"), which requires, among other provisions, the assignment of patent rights to any invention made during your employment at the Company and non-disclosure of Company confidential information. A copy of the CIIAA is attached hereto. Please note that we must receive your signed CIIAA on or before your first day of employment with the Company.

8. General. This Offer Letter together with the CIIAA and the Officer Agreements, when signed by you, set forth the terms of your employment with the Company and supersede any and all prior representations and agreements including, but not limited to, any representations made during your recruitment, interviews, or pre-employment negotiations, whether written or oral. In the event of a conflict between the terms and provisions of this Offer Letter and the CIIAA, Officer Employee Agreement or Stock Agreements, the terms and provisions of the CIIAA, Officer Employee Agreement and Stock Agreements will control. Any amendment of this Offer Letter or any waiver of a right under this Offer Letter must be in a writing signed by you and the President and Chief Executive Office of the Company. California law will govern this Offer Letter.

This Offer Letter is contingent upon the satisfactory completion of reference and background checks, along with verification of any previous employment, degree(s), or certification(s) that you included on your resume. If the results of the reference or background checks are unsatisfactory, or if the Company is unable to verify your previous employment, degree(s), or certification(s), the Company reserves the right to rescind this offer at any time.

9. Confidential Offer of Employment. Until you have accepted this offer of employment, it is strictly confidential and its contents should only be disclosed and discussed with your significant other, attorney, accountant, and/or tax advisor.

To accept the Company's offer of employment, please sign and date this letter in the space provided below. This offer of employment will terminate if the Offer Letter is not accepted, signed, and returned by you to the Company on or before November 5, 2021. We look forward to your favorable reply and to working with you at Caribou Biosciences, Inc.

Sincerely

/s/ Barbara G. McClung for
Rachel E. Haurwitz, Ph.D.
President and CEO

AGREED TO AND ACCEPTED:

Signature:	/s/ Syed Rizvi
Printed Name:	Syed Risvi
Date:	October 30th, 2021

Enclosures:

Description of Benefits
Confidential Information and Invention Assignment Agreement
Officer Employment Agreement
Indemnification Agreement

Exhibit 10.42

OFFICER EMPLOYMENT AGREEMENT

This Officer Employment Agreement ("Agreement") is dated as of January 18, 2022 ("Effective Date"), and is by and between Caribou Biosciences, Inc., a Delaware corporation, having an address at 2929 7th Street, Suite 105, Berkeley, CA 94710 (the "Company"), and Syed Rizvi, M.D. (the "Officer").

WHEREAS, the Company desires to employ the Officer and the Officer desires to be employed by the Company on the terms and conditions contained herein.

NOW, THEREFORE, in consideration of the mutual covenants and agreements herein contained and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties agree as follows:

1. Employment.

a. Term. The term of this Agreement shall commence on the Effective Date and continue until terminated in accordance with the provisions hereof (the "Term").

b. Position and Duties. During the Term, the Officer shall serve as Chief Medical Officer of the Company and shall have supervision and control over and responsibility for the day-to-day business and affairs of the Company as may from time to time be prescribed by the Company's President and Chief Executive Officer, provided that such duties are consistent with the Officer's position or other positions that they may hold from time to time. The Officer shall devote substantially all of their full working time and efforts to the business of the Company. Notwithstanding the foregoing, the Officer may serve on other boards of directors, with the approval of the Board, or sit on the governing boards of, or hold leadership positions related to community, charitable, academic, and religious activities, as long as such services and activities are disclosed to the Board and do not materially interfere with the Officer's performance of their duties to the Company as provided in this Agreement.

2. Compensation and Related Matters.

a. Base Salary. During the Term, the Officer's initial annual base salary shall be $490,000.00. The Officer's base salary shall be reviewed from time to time by the Company's Board of Directors ("Board") or the Compensation Committee of the Board. The base salary in effect at any given time is referred to herein as "Base Salary." The Base Salary shall be payable in a manner that is consistent with the Company's usual payroll practices.

b. Incentive Compensation. During the Term, the Officer shall be eligible to receive cash incentive compensation as determined by the Board or the Compensation Committee from time to time. The Officer's initial target annual incentive compensation shall be 40% of their Base Salary. Except as otherwise provided herein, to earn incentive compensation, the Officer must be employed by the Company on the day such incentive compensation is paid.

c. Company Benefits. The Officer shall be entitled to all benefits received by employees of the Company in accordance with the Company's policies and plans.

3. **Termination.** During the Term, the Officer's employment hereunder may be terminated without any breach of this Agreement under the following circumstances:

a. Termination by the Company for Cause. The Company may terminate the Officer's employment hereunder for Cause. For purposes of this Agreement, "Cause" shall mean: (i) conduct by the Officer constituting a material act of misconduct in connection with the performance of their duties, including, without limitation, misappropriation of funds or property of the Company or any of its subsidiaries or affiliates other than the occasional, customary, and de minimis use of Company property for personal purposes; (ii) the commission by the Officer of any felony or a misdemeanor involving moral turpitude, deceit, dishonesty or fraud, or any conduct by the Officer that would reasonably be expected to result in material injury or reputational harm to the Company or any of its subsidiaries and affiliates if they were retained in their position; (iii) continued non-performance by the Officer of their duties hereunder (other than by reason of the Officer's physical or mental illness, incapacity or disability) that has continued for more than 30 days following written notice of such non-performance from the Board; (iv) a material violation by the Officer of the Company's written policies; or (v) failure to cooperate with a bona fide internal investigation or an investigation by regulatory or law enforcement authorities, after being instructed by the Company to cooperate, or the willful destruction or failure to preserve documents or other materials known to be relevant to such investigation or the inducement of others to fail to cooperate or to produce documents or other materials in connection with such investigation.

b. Termination by the Company Without Cause. The Company may terminate the Officer's employment hereunder at any time without Cause upon written notice of such termination ("Notice of Termination"). Any termination by the Company of the Officer's employment under this Agreement which does not constitute a termination for Cause under Section 3(a) and does not result from the death or disability of the Officer under Section 3(d) or (e), respectively, shall be deemed a termination without Cause.

c. Termination by the Officer. The Officer may terminate their employment hereunder at any time for any reason, including but not limited to Good Reason. For purposes of this Agreement, "Good Reason" shall mean that the Officer has complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following events: (i) a material diminution in the Officer's responsibilities, authority or duties; (ii) the assignment of duties to the Officer that are materially inconsistent with their position; (iii) a decrease of more than 10% of the Officer's Base Salary except for across-the-board salary reductions based on the Company's financial performance similarly affecting all officers of the Company; (iv) a change by the Company in the Company location at which the Officer performs their duties to a location that is more than 50 miles (driving distance) from the original location; or (v) the material breach of this Agreement by the Company. "Good Reason Process" shall mean that (i) the Officer reasonably determines in good faith that a "Good Reason" condition has occurred; (ii) the Officer notifies the Company in writing of the first occurrence of the Good Reason condition within 30 days of the first occurrence of such condition; (iii) the Officer cooperates in good faith with the Company's efforts, for a period of 30 days following such notice (the "Cure Period"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) the Officer terminates their employment within 30 days after the end of the Cure Period. If the Company cures the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred.

d. Death. The Officer's employment hereunder shall terminate upon their death.

e. Disability. The Company may terminate the Officer's employment if they are disabled and unable to perform the essential functions of the Officer's then existing position or positions under this Agreement with or without reasonable accommodation for a period of 180 days (which need not be consecutive) in any 12-month period and the Company shall provide a Notice of Termination at that time. If any question shall arise as to whether during any period the Officer is disabled so as to be unable to perform the essential functions of the Officer's then existing position or positions with or without reasonable accommodation, the Officer may, and at the request of the Company shall, submit to the Company a certification in reasonable detail by a physician selected by the Company to whom the Officer or the Officer's guardian has no reasonable objection as to whether the Officer is so disabled or how long such disability is expected to continue, and such certification shall for the purposes of this Agreement be conclusive of the issue. The Officer shall cooperate with any reasonable request of the physician in connection with such certification. If such question shall arise and the Officer shall fail to submit such certification, the Company's determination of such issue shall be binding on the Officer. Nothing in this Section 3(b) shall be construed to waive the Officer's rights, if any, under existing federal and state law including, without limitation, the Family and Medical Leave Act of 1993, 29 U.S.C. §2601 , et seq. and the Americans with Disabilities Act, 42 U.S.C. §12101 , et seq.

f. Notice of Termination. Except for termination as specified in Section 3(d), any termination of the Officer's employment by the Company or any such termination by the Officer shall be communicated by written Notice of Termination to the other party hereto. For purposes of this Agreement, a "Notice of Termination" shall mean a written notice which shall indicate the specific termination provision in this Agreement relied upon.

g. Date of Termination. "Date of Termination" shall mean: (i) if the Officer's employment is terminated by the Company for Cause under Section 3(a) or without Cause under Section 3(b) or on account of disability under Section 3(e), the date on which Notice of Termination is given; (ii) if the Officer's employment is terminated by the Officer under Section 3(c) without Good Reason, 30 days after the date on which a Notice of Termination is given; (iii) if the Officer's employment is terminated by the Officer under Section 3(c) with Good Reason, the date on which a Notice of Termination is given after the end of the Cure Period; and (iv) if the Officer's employment is terminated by their death, the date of their death. Notwithstanding the foregoing, in the event that the Officer gives a Notice of Termination to the Company under Section 3(c), the Company may unilaterally and solely at its own discretion accelerate the Date of Termination and such acceleration shall not result in a termination by the Company for purposes ofthis Agreement; provided, however, that in no event shall such accelerated Date of Termination be earlier than the date on which the Notice of Termination is delivered to the Company.

4. Compensation Upon Termination.

a. Termination Generally. If the Officer's employment with the Company is terminated for any reason, the Company shall pay or provide to the Officer (or to their authorized representative or estate) (i) any Base Salary earned through the Date of Termination, unpaid expense reimbursements in accordance with Company policy, and unused vacation that accrued through the Date of Termination on or before the time required by law but in no event more than 30 days after the Officer's Date of Termination; and (ii) any vested benefits the Officer may have under any employee benefit plan of the Company through the Date of Termination, which vested benefits shall be paid and/or provided in accordance with the terms of such employee benefit plans (collectively, the "Accrued Benefit").

b. Termination by the Company Without Cause or by the Officer with Good Reason. During the Term, if the Officer's employment is terminated by the Company without Cause as provided in Section 3(b), or the Officer terminates their employment for Good Reason as provided in Section 3(c), then the Company shall provide the Officer with the Accrued Benefit and the compensation and benefits set forth in this Section 4(b), the latter subject to the Officer signing a separation agreement containing, among other provisions, a general release of claims in favor of the Company and related persons and entities, confidentiality, return of property, and non-disparagement, in a form and manner satisfactory to the Company (the "Separation Agreement and Release") and the Separation Agreement and Release becoming fully effective, all within the time frame set forth in the Separation Agreement and Release: (i) the Company shall pay the Officer an amount equal to 9 months of the Officer's Base Salary (the "Severance Amount"); (ii) if the Officer (and their dependents, if applicable) was participating in the Company's group health plans immediately prior to the Date of Termination and the Officer elects

COBRA health continuation for their self (and their dependents, if applicable), then the Company shall pay for 9 months or the Officer's COBRA health continuation period, whichever ends earlier, the COBRA health contribution that the Company would have made to provide health insurance to the Officer (and their dependents, if applicable) if the Officer had remained employed by the Company; provided, however, that the Company shall only be required to pay that percentage of dependent health insurance that the Company would be paying if the Officer had remained employed by the Company; and (iii) the amounts payable under Sections 4(b)(i) and (ii) shall be paid out in substantially equal installments in accordance with the Company's payroll practice over 9 months commencing on the first regularly scheduled payroll date that is at least 30 days after the Date of Termination, provided that the Separation Agreement and Release becomes fully effective; provided, however, that the initial payment shall include a catch-up payment to cover amounts retroactive to the day immediately following the Date of Termination. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2).

c. Change in Control. During the Term, if within 12 months after a Change in Control as defined herein, or within three months prior to a 409A Change in Control as defined herein, the Officer's employment is terminated by the Company without Cause as provided in Section 3(b) or the Officer terminates their employment for Good Reason as provided in Section 3(c), then, subject to the signing of the Separation Agreement and Release by the Officer and the Separation Agreement and Release becoming fully effective all within the time frame set forth in the Separation Agreement and Release, the Officer shall receive the benefits set forth in Section 4(b)(i) and (ii), and 100% of the Officer's then unvested stock options and time-based restricted stock shall become immediately vested; provided, however, that the number of months of base salary and benefits continuation in Sections 4(b)(i) and (ii) shall be increased to 12 months and the Officer shall also be provided with one times their target bonus amount for the year in which the Date of Termination occurs, which target bonus amount is payable in a lump sum on the first regularly scheduled payroll date that is at least 30 days following the Date of Termination or, if the Officer's employment was terminated within three months prior to a 409A Change in Control, upon the 409A Change in Control; provided, further that notwithstanding the language in Section 4(b)(iii), if the Change in Control is a change in the ownership or effective control of the Company, or in the ownership of a substantial portion of the Company's assets under Section 409A of the Code (a "409A Change in Control"), then the Severance Amount set forth in Section 4(b)(i) shall be payable as a lump sum on the first regularly scheduled payroll date that is at least 30 days following the Date of Termination, subject to the Separation Agreement and Release having become fully effective (for clarity, the COBRA payments set forth in Section 4(b)(ii) shall be paid in accordance with Section 4(b)(iii)) or, if the Officer's employment was terminated within three months prior to a 409A Change in Control, upon the 409A Change in Control. For purposes of this Section 4(c), "Change in Control" shall mean any of the following: (i) any "person," as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended (the "Act") (other than the Company, any of its subsidiaries, or any trustee, fiduciary or other person or entity holding securities under any employee benefit plan or trust of the Company or any of its subsidiaries), together with all "affiliates" and "associates" (as such terms are defined in Rule 12b-2 under the Act) of such person, shall become the "beneficial owner" (as such tem1 is defined in Rule 13d-3 under the Act), directly or indirectly, of securities of the Company representing 50% or more of the combined voting power of the Company's then outstanding securities having the right to vote in an election of the Board ("Voting Securities") (in such case other than as a result of an acquisition of securities directly from the Company); or (ii) the date a majority of the members of the Board is replaced during any 12-month period by directors whose appointment or election is not endorsed by a majority of the members of the Board before the date of the appointment or election; or (iii) the consummation of (A) any consolidation or merger of the Company where the stockholders of the Company, immediately prior to the consolidation or merger, would not, immediately after the consolidation or merger, beneficially own (as such term is defined in Rule 13d-3 under the Act), directly or indirectly, shares representing in the aggregate more than 50% of the voting shares of the Company issuing cash or securities in the consolidation or merger (or of its ultimate parent corporation, if any), or (B) any sale or other transfer (in one transaction or a series of transactions contemplated or arranged by any party as a single plan) of all or substantially all of the assets of the Company. Notwithstanding the foregoing, a "Change in Control" shall not be deemed to have occurred for purposes of the foregoing clause solely as the result of an acquisition of securities by the Company that, by reducing the number of shares of Voting Securities outstanding, increases the proportionate number of Voting Securities beneficially owned by any person to 50% or more of the combined voting power of all of the then outstanding Voting Securities; provided, however, that if any person referred to in this sentence shall thereafter become the beneficial owner of any additional shares of Voting Securities (other than pursuant to a stock split, stock dividend, or similar transaction or as a result of an acquisition of securities directly from the Company) and immediately thereafter beneficially owns 50% or more of the combined voting power of all of the then outstanding Voting Securities, then a "Change in Control" shall be deemed to have occurred.

5. Additional Limitations and Section 409A.

a. Additional Limitations. Notwithstanding anything to the contrary in this Agreement, in the event that the amount of any compensation, payment or distribution by the Company to or for the benefit of the Officer, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a manner consistent with Section 2800 of the Internal Revenue Code of 1986, as amended (the "Code"), and the applicable regulations thereunder (the "Aggregate Payments"), would be subject to the excise tax imposed by Section 4999 of the Code, then the Aggregate Payments shall be reduced (but not below zero) so that the sum of all of the Aggregate Payments shall be $1 .00 less than the amount at which the Officer becomes subject to the excise tax imposed by Section 4999 of the Code; provided that such reduction shall only occur if it would result in the Officer receiving a higher After Tax Amount (as defined below) than the Officer would receive if the Aggregate Payments were not subject to such reduction. In such event, the Aggregate Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Aggregate Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 2800 of the Code: (1) cash payments not subject to Section 409A of the Code; (2) cash payments subject to Section 409A of the Code; (3) equity-based payments and acceleration; and (4) non-cash forms of benefits; provided that in the case of all the foregoing Aggregate Payments all amounts or payments that are not subject to calculation under Treas. Reg. §1.2800-1 , Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. § 1.2800-1 , Q&A-24(b) or (c). For purposes of this Section S(a), the "After Tax Amount" means the amount of the Aggregate Payments less all federal, state, and local income, excise and employment taxes imposed on the Officer as a result of the Officer's receipt of the Aggregate Payments. For purposes of determining the After Tax Amount, the Officer shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes. The determination as to whether a reduction in the Aggregate Payments shall be made pursuant to Section S(b)(i) shall be made by a nationally recognized accounting firm selected by the Company (the "Accounting Firm"), which shall provide detailed supporting calculations both to the Company and the Officer within 15 business days of the Date of Termination, if applicable, or at such earlier time as is reasonably requested by the Company or the Officer. Any determination by the Accounting Firm shall be binding upon the Company and the Officer.

b. Section 409A. Notwithstanding anything to the contrary in this Agreement, if at the time of the Officer's separation from service within the meaning of Section 409A of the Code, the Company determines that the Officer is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that the Officer becomes entitled to under this Agreement on account of the Officer's separation from service would be considered deferred compensation otherwise subject to the 20% additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) 6 months and one day after the Officer's separation from service or (B) the Officer's death. If any such delayed cash payment is otherwise payable on an installment basis, the first payment shall include a catch-up payment covering amounts that would otherwise have been paid during the six-month period but for the application of this provision, and the balance of the installments shall be payable in accordance with their original schedule. All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by the Officer during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year (except for any lifetime or other aggregate limitation applicable to medical expenses). Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit. To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon the Officer's termination of employment, then such payments or benefits shall be payable only upon the Officer's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-l (h). The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. The parties agree that this Agreement may be amended, as reasonably

requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party. The Company makes no representation or warranty and shall have no liability to the Officer or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section 409A.

6. **Litigation and Regulatory Cooperation.** During and after the Term, the Officer shall cooperate fully with the Company in the defense or prosecution of any claims or actions now in existence or which may be brought in the future against or on behalf of the Company that relate to events or occurrences that transpired while the Officer was employed by the Company. The Officer's full cooperation in connection with such claims or actions shall include, but not be limited to, being available to meet with counsel to prepare for discovery or trial and to act as a witness on behalf of the Company at mutually convenient times. During and after the Term, the Officer also shall cooperate fully with the Company in connection with any investigation or review of any federal, state or local regulatory authority as any such investigation or review relates to events or occurrences that transpired while the Officer was employed by the Company. The Company shall reimburse the Officer for any reasonable out-of-pocket expenses incurred in connection with the Officer's performance of obligations pursuant to this Section 6 and, after their employment with the Company terminates, the Officer may be entitled for reasonable compensation for their time. For the avoidance of doubt, nothing in this Agreement shall be interpreted or applied to prohibit the Officer from making any good faith report to any governmental agency or other governmental entity concerning any act or omission that the Officer reasonably believes constitutes a possible violation of federal or state law or making other disclosures that are protected under the anti-retaliation or whistleblower provisions of applicable federal or state law or regulation.

7. **Relief.** The Officer agrees that it would be difficult to measure any damages caused to the Company which might result from any breach by the Officer of this Agreement, and that in any event money damages would be an inadequate remedy for any such breach. Accordingly, the Officer agrees that if the Officer breaches, or proposes to breach, this Agreement, the Company shall be entitled, in addition to all other remedies that it may have, to an injunction or other appropriate equitable relief to restrain any such breach without showing or proving any actual damage to the Company. In addition, in the event the Officer breaches the Confidential Information and Invention Assignment Agreement, effective as of November 8, 2021, by and between the Company and the Officer ("CIIA"), during a period when they are receiving severance payments pursuant to Section 4(b) or (c), the Company shall have the right to suspend or terminate such severance payments. Such suspension or termination shall not limit the Company's other options with respect to relief for such breach and shall not relieve the Officer of their duties under this Agreement.

8. **Governing Law and Jurisdiction.** This Agreement shall be governed by the laws of the State of California, and the parties hereby consent to the jurisdiction of the state and federal courts in the State of California.

9. **Integration.** This Agreement constitutes the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior agreements between the parties concerning such subject matter, with the sole exception of the CIIA and the Indemnification Agreement, dated November 8, 2021, both by and between the Company and the Officer. If there are any conflicts between the terms and conditions of the CIIA and this Agreement, the terms and conditions of this Agreement shall govern.

10. **Successor to the Officer.** This Agreement shall inure to the benefit of and be enforceable by the Officer's personal representatives, executors, administrators, heirs, distributees, devisees and legatees. In the event of the Officer's death after their termination of employment but prior to the completion by the Company of all payments due them under this Agreement, the Company shall continue such payments to the Officer's beneficiary designated in writing to the Company prior to their death (or to their estate, if the Officer fails to make such designation).

11. **Enforceability.** lf any portion or provision of this Agreement (including, without limitation, any portion or provision of any section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby,

and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

12. **Survival.** The provisions of this Agreement shall survive the termination of this Agreement and/or the termination of the Officer's employment to the extent necessary to effectuate the terms contained herein.

13. **Waiver.** No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement, or the waiver by any party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

14. **Notices.** Any notices, requests, demands and other communications provided for by this Agreement shall be sufficient if in writing and delivered in person or sent by a nationally recognized overnight courier service or by registered or certified mail, postage prepaid, return receipt requested, to the Officer at the last address the Officer has filed in writing with the Company or, in the case of the Company, at the address set forth above to the President and Chief Executive Officer with a copy to legalnotices@cariboubio.com; provided that if the Officer providing notice is the President and Chief Executive Officer, they are not required to provide notice to themself but instead shall provide written notice to the Chief Legal Officer.

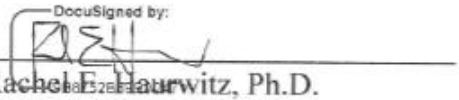
15. **Amendment.** This Agreement may be amended or modified only by a written instrument signed by the Officer and by a duly authorized representative of the Company.

16. **Successor to Company.** The Company shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business or assets of the Company expressly to assume and agree to perform this Agreement to the same extent that the Company would be required to perform it if no succession had taken place. Failure of the Company to obtain an assumption of this Agreement at or prior to the effectiveness of any succession shall be a material breach of this Agreement.

17. **Counterparts.** This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original; but such counterparts shall together constitute one and the same document.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the Effective Date.

Caribou Biosciences, Inc.

By: 

Name: Rachel E. Haurwitz, Ph.D.
Title: President and CEO

Syed Rizvi, M.D.

By: 

Exhibit 10.46

AMENDMENT TO CARIBOU BIOSCIENCES, INC.
2013 EQUITY INCENTIVE PLAN

Effective December 9, 2021, the following paragraphs of the Caribou Biosciences, Inc. 2013 Equity Incentive Plan, as amended and restated as of April 3, 2019, (the "Plan") are amended to read as follows, with amendments marked as indicated:

13. Limited Transferability of Shares Underlying Awards

(a) General. Notwithstanding anything to the contrary, until the Company becomes subject to the reporting requirements of Section 13 or 15(d) of the Exchange Act, or after the Administrator determines that it is, will, or may no longer be relying upon the exemption from registration under the Exchange Act as set forth in Rule 12h-1(f) promulgated under the Exchange Act, no Participant or other stockholder shall Transfer (as such term is defined below) any Shares (or any rights of or interests in such Shares) acquired pursuant to the Plan and/or any Award to any person or entity unless such Transfer is approved by the Company prior to such Transfer, which approval may be granted or withheld in the Company's sole and absolute discretion. "Transfer" shall mean, with respect to any security, the direct or indirect assignment, sale, transfer, tender, pledge, hypothecation, or the grant, creation or suffrage of a lien or encumbrance in or upon, or the gift, placement in trust, or the Constructive Sale (as such term is defined below) or other disposition of such security (including transfer by testamentary or intestate succession, merger or otherwise by operation of law) or any right, title or interest therein (including, but not limited to, any right or power to vote to which the holder thereof may be entitled, whether such right or power is granted by proxy or otherwise), or the record or beneficial ownership thereof, the offer to make such a sale, transfer, Constructive Sale or other disposition, and each agreement, arrangement or understanding, whether or not in writing, to effect any of the foregoing. "Constructive Sale" shall mean, with respect to any security, a short sale with respect to such security, entering into or acquiring an offsetting derivative contract with respect to such security, entering into or acquiring a futures or forward contract to deliver such security, or entering into any other hedging or other derivative transaction that has the effect of materially changing the economic benefits and risks of ownership. Any purported Transfer effected in violation of this Section 13 shall be null and void and shall have no force or effect and the Company shall not be required (i) to transfer on its books any Shares that have been sold or otherwise transferred in violation of any of the provisions of the Plan or (ii) to treat as owner of such Shares or to accord the right to vote or pay dividends to any purchaser or other transferee to whom such Shares shall have been so transferred.

(b) Approval Process. Any Participant or stockholder seeking the approval of the Company to Transfer some or all of its Shares shall give written notice thereof to the Secretary of the Company that shall include: (1) the name of the stockholder; (2) the proposed transferee; (3) the number of shares of the Transfer of which approval is thereby requested; and (4) the purchase price, if any, of the shares proposed for Transfer. The Company may require the Participant to supplement its notice with such additional information as the Company may request or as may otherwise be required by the applicable Award Agreement or other applicable written agreement. In addition, such request for Transfer shall be subject to such right of first

refusal, transfer provisions and any other terms and conditions as may be set forth in the applicable Award Agreement or other applicable written agreement.

CARIBOU BIOSCIENCES, INC.

2021 EQUITY INCENTIVE PLAN

STOCK OPTION AGREEMENT

Unless otherwise defined herein, the terms defined in the 2021 Equity Incentive Plan (the "Plan") shall have the same defined meanings in this Stock Option Agreement (the "Option Agreement").

I. NOTICE OF STOCK OPTION GRANT

Name:

Address:

The undersigned (the "Participant") has been granted an Option to purchase Common Stock of the Company, subject to the terms and conditions of the Plan and this Option Agreement, as follows:

Date of Grant:	[_____]
Vesting Commencement Date:	_____
Exercise Price per Share:	$[ ]
Total Number of Shares Represented by stock option:	_____
Total Exercise Price:	$ _____
Type of Option:	_____ Incentive Stock Option _____ Nonqualified Stock Option
Term/Expiration Date:	[_____]

Vesting Schedule:

This Option shall be exercisable, in whole or in part, according to the following vesting schedule:

[Vesting schedule], subject to Participant continuing to be an Employee through each such date. On each vesting date, the number of Shares vesting shall be rounded down to the nearest whole share, with the balance vesting on the last vesting date.

Termination Period:

This Option, to the extent vested, shall be exercisable for three (3) months after Participant ceases to be an Employee, unless such termination is due to Participant's death or disability, in which case this Option shall be exercisable for twelve (12) months after Participant ceases to be an Employee. Notwithstanding the foregoing sentence, in no event may this Option be exercised after the Term/Expiration Date as provided above and this Option may be subject to earlier termination as provided in Section 14 of the Plan.

II. AGREEMENT

1. Grant of Option. The Administrator hereby grants to the Participant an option (the "Option") to purchase the number of Shares set forth in Section I of this Stock Option Agreement, at the exercise price per Share set forth in Section I of this Stock Option Agreement (the "Exercise Price"), and subject to the terms and conditions of the Plan, which is incorporated herein by reference. Subject to Article 14 of the Plan, in the event of a conflict between the terms and conditions of the Plan and this Option Agreement, the terms and conditions of the Plan shall prevail.

If this Option has been designated in Section I of this Option Agreement as an Incentive Stock Option ("ISO"), this Option is intended to qualify as an Incentive Stock Option as defined in Section 422 of the Code. Nevertheless, to the extent that it exceeds the $100,000 rule of Code Section 422(d), that portion of the Option shall be treated as a Nonqualified Stock Option ("NSO"). Further, if for any reason this Option (or portion thereof) shall not qualify as an ISO, then, to the extent of such nonqualification, such Option (or portion thereof) shall be regarded as a NSO granted under the Plan. In no event shall the Administrator, the Company or any Parent or Subsidiary or any of their respective employees or directors have any liability to Participant (or any other person) due to the failure of the Option to qualify for any reason as an ISO.

2. Exercise of Option.

(a) Right to Exercise. This Option shall be exercisable during its term in accordance with the Vesting Schedule set forth in Section I of this Stock Option Agreement and with the applicable provisions of the Plan and this Option Agreement.

(b) Method of Exercise. This Option shall be exercisable by delivery of an exercise notice in the form attached as Exhibit A (the "Exercise Notice") or in a manner and pursuant to such procedures as the Administrator may determine, which shall state the election to exercise the Option, the number of Shares with respect to which the Option is being exercised (the "Exercised Shares"), and such other representations and agreements as may be required by the Company. The Exercise Notice shall be accompanied by payment of the aggregate Exercise Price as to all Exercised Shares, together with any applicable tax withholding. This Option shall be deemed to be exercised upon receipt by the Company of such fully executed Exercise Notice accompanied by the aggregate Exercise Price, together with any applicable tax withholding.

No Shares shall be issued pursuant to the exercise of an Option unless such issuance and such exercise comply with Applicable Laws. Assuming such compliance, for income tax purposes the Shares shall be considered transferred to Participant on the date on which the Option is exercised with respect to such Shares.

[Historical Lock-Up: 3. Lock-Up Period. Participant agrees to execute and deliver the lock-up agreement attached hereto as Exhibit B (the "Lock-Up Agreement"). Participant agrees that any transferee of the Option or shares acquired pursuant to the Option shall be bound by this Section 3 and the Lock-Up Agreement.]

4. Method of Payment. Payment of the aggregate Exercise Price shall be by any of the methods permitted in Section 12.1 of the Plan, or a combination thereof, at the election of the Participant and as permitted by the Administrator.

5. Restrictions on Exercise. This Option may not be exercised if the issuance of such Shares upon such exercise or the method of payment of consideration for such shares would constitute a violation of any Applicable Law.

6. Non-Transferability of Option. This Option may not be transferred in any manner otherwise than by will or by the laws of descent or distribution and may be exercised during the lifetime of Participant only by Participant (subject to Section 3 of the Option Agreement). The terms of the Plan and this Option Agreement shall be binding upon the executors, administrators, heirs, successors, and assigns of Participant.

7. Term of Option. This Option may be exercised only within the term set out in Section I of this Option Agreement and may be exercised during such term only in accordance with the Plan and the terms of this Option Agreement. Except as may otherwise be provided in any employment agreement, in the event of any transaction or

Change in Control (as defined in the Plan), the Option may, in the discretion of the Administrator, be terminated, which may be in exchange for cash or property, be assumed or substituted by the successor corporation or otherwise continued in full force and effect pursuant to the terms of the Change in Control or other transaction on such terms and conditions as the Administrator determines.

8. Tax Obligations.

(a) Tax Withholding. Participant agrees to make appropriate arrangements with the Company (or the Parent or Subsidiary employing or retaining Participant) for the satisfaction of all Federal, state, local, and foreign income and employment tax withholding requirements applicable to the Option exercise. Participant acknowledges and agrees that the Company may refuse to honor the exercise and refuse to deliver the Shares if such withholding amounts are not delivered at the time of exercise.

(b) Notice of Disqualifying Disposition of ISO Shares. If the Option granted to Participant herein is an ISO, and if Participant sells or otherwise disposes of any of the Shares acquired pursuant to the ISO on or before the later of (i) the date two (2) years after the Date of Grant, or (ii) the date one (1) year after the date of exercise, Participant shall immediately notify the Company in writing of such disposition. Participant agrees that Participant may be subject to income tax withholding by the Company on the compensation income recognized by Participant.

9. Entire Agreement; Governing Law. The Plan is incorporated herein by reference. The Plan and this Option Agreement constitute the entire agreement of the parties with respect to the subject matter hereof and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof and may not be modified adversely to the Participant's interest except by means of a writing signed by the Company and Participant. This Option Agreement is governed by the internal substantive laws but not the choice of law rules of Delaware.

10. No Guarantee of Continued Service. PARTICIPANT ACKNOWLEDGES AND AGREES THAT THE VESTING OF SHARES PURSUANT TO THE VESTING SCHEDULE HEREOF IS EARNED ONLY BY CONTINUING AS AN EMPLOYEE AT THE WILL OF THE COMPANY (OR THE PARENT OR SUBSIDIARY EMPLOYING OR RETAINING PARTICIPANT) AND NOT THROUGH THE ACT OF BEING HIRED, BEING GRANTED THIS OPTION, OR ACQUIRING SHARES HEREUNDER. PARTICIPANT FURTHER ACKNOWLEDGES AND AGREES THAT THIS AGREEMENT, THE TRANSACTIONS CONTEMPLATED HEREUNDER, AND THE VESTING SCHEDULE SET FORTH HEREIN DO NOT CONSTITUTE AN EXPRESS OR IMPLIED PROMISE OF CONTINUED ENGAGEMENT AS AN EMPLOYEE FOR THE VESTING PERIOD, FOR ANY PERIOD, OR AT ALL, AND SHALL NOT INTERFERE IN ANY WAY WITH PARTICIPANT'S RIGHT OR THE RIGHT OF THE COMPANY (OR THE PARENT OR SUBSIDIARY EMPLOYING OR RETAINING PARTICIPANT) TO TERMINATE PARTICIPANT'S RELATIONSHIP AS AN EMPLOYEE AT ANY TIME, WITH OR WITHOUT CAUSE.

Participant acknowledges receipt of a copy of the Plan and represents that they are familiar with the terms and provisions thereof, and hereby accepts this Option subject to all of the terms and provisions thereof. Participant has reviewed the Plan and this Option in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Option, and fully understands all provisions of the Option. Participant hereby agrees to accept as binding, conclusive, and final all decisions or interpretations of the Administrator upon any questions arising under the Plan or this Option. Participant further agrees to notify the Company upon any change in the residence address indicated below.

PARTICIPANT	CARIBOU BIOSCIENCES, INC.
Signature	By
«Name»	
Print Name	Print Name
	Title
Residence Address	

EXHIBIT A

2021 EQUITY INCENTIVE PLAN

EXERCISE NOTICE

Caribou Biosciences, Inc.
2929 7th Street, Suite 105
Berkeley, CA 94710

Attention: President

1. Exercise of Option. Effective as of today, , , the undersigned ("Participant") hereby elects to exercise Participant's option (the "Option") to purchase shares of the Common Stock (the "Shares") of Caribou Biosciences, Inc. (the "Company") under and pursuant to the 2021 Equity Incentive Plan (the "Plan") and the Stock Option Agreement dated, , (the "Option Agreement").

2. Delivery of Payment. Participant herewith delivers to the Company the full purchase price of the Shares, as set forth in the Option Agreement, and any and all withholding taxes due in connection with the exercise of the Option, using a method provided in Section 12.1 of the Plan, as may be permitted by the Administrator.

3. Representations of Participant. Participant acknowledges that Participant has received, read, and understood the Plan and the Option Agreement and agrees to abide by and be bound by their terms and conditions.

4. Rights as Stockholder. Until the issuance of the Shares (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company), no right to vote or receive dividends or any other rights as a stockholder shall exist with respect to the Common Stock subject to an Award, notwithstanding the exercise of the Option. The Shares shall be issued to Participant as soon as practicable after the Option is exercised in accordance with the Option Agreement. No adjustment shall be made for a dividend or other right for which the record date is prior to the date of issuance except as provided in Section 13 of the Plan.

5. Tax Consultation. Participant understands that Participant may suffer adverse tax consequences as a result of Participant's purchase or disposition of the Shares. Participant represents that Participant has consulted with any tax consultants Participant deems advisable in connection with the purchase or disposition of the Shares and that Participant is not relying on the Company for any tax advice.

6. Successors and Assigns. The Company may assign any of its rights under this Exercise Notice to single or multiple assignees, and this Exercise Notice shall inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer herein set forth, this Exercise Notice shall be binding upon Participant and their heirs, executors, administrators, successors, and assigns.

7. Interpretation. Any dispute regarding the interpretation of this Exercise Notice shall be submitted by Participant or by the Company forthwith to the Administrator, which shall review such dispute at its next regular meeting. The resolution of such a dispute by the Administrator shall be final and binding on all parties.

8. Governing Law; Severability. This Exercise Notice is governed by the internal substantive laws, but not the choice of law rules, of Delaware. In the event that any provision hereof becomes or is declared by a court of competent jurisdiction to be illegal, unenforceable, or void, this Exercise Notice shall continue in full force and effect.

9. Entire Agreement. The Plan and Option Agreement are incorporated herein by reference. This Exercise Notice, the Plan, and the Option Agreement constitute the entire agreement of the parties with respect to the subject matter hereof and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof and may not be modified adversely to the Participant's interest except by means of a writing signed by the Company and Participant.

Submitted by:	Accepted by:
PARTICIPANT	CARIBOU BIOSCIENCES, INC.
Signature	By
Print Name	Print Name
	Title
Address:	Address:
	2929 7th Street, Suite 105
	Berkeley, CA 94710
	Date Received

[EXHIBIT B

_____, 2021

BofA Securities, Inc.
Citigroup Global Markets Inc.
SVB Leerink LLC

as Representatives of the several
Underwriters to be named in the
within-mentioned Underwriting Agreement

c/o BofA Securities, Inc.
One Bryant Park
New York, New York 10036

Citigroup Global Markets Inc.
388 Greenwich Street
New York, New York 10013

SVB Leerink LLC
One Federal Street, 37th Floor
Boston, Massachusetts 02110

Re: Proposed Public Offering by Caribou Biosciences, Inc.

Dear Ladies and Gentlemen:

The undersigned, a stockholder and/or a stock option holder and/or an officer and/or a director, as applicable, of Caribou Biosciences, Inc., a Delaware corporation (the "**Company**"), understands that BofA Securities, Inc., Citigroup Global Markets Inc. and SVB Leerink LLC (collectively, the "**Representatives**") previously entered into an Underwriting Agreement, dated July 22, 2021 (the "**Underwriting Agreement**") with the Company and the other underwriters party thereto providing for the public offering (the "**Public Offering**") of shares of the Company's common stock, par value $0.0001 per share (the "**Common Stock**"). In recognition of the benefit that the Public Offering has conferred upon the undersigned as a stockholder and/or a stock option holder and/or an officer and/or a director, as applicable, of the Company, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the undersigned agrees with each underwriter named in the Underwriting Agreement that, during the period beginning on the date hereof and ending on the date that is 180 days from the date of the Underwriting Agreement (the "**Lock-Up Period**"), the undersigned will not, without the prior written consent of the Representatives, (i) directly or indirectly, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of any shares of the Company's Common Stock or any securities convertible into or exercisable or

exchangeable for shares of Common Stock, whether now owned or hereafter acquired by the undersigned or with respect to which the undersigned has or hereafter acquires the power of disposition (collectively, the "**Lock-Up Securities**"), or exercise any right with respect to the registration of any of the Lock-Up Securities, or file, cause to be filed or cause to be confidentially submitted any registration statement in connection therewith, under the Securities Act of 1933, as amended, (ii) enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of the Lock-Up Securities, whether any such swap or transaction is to be settled by delivery of shares of Common Stock or other securities, in cash or otherwise or (iii) publicly disclose the intention to do any of the foregoing described in clauses (i) and (ii) above. If the undersigned is an officer or director of the Company, the undersigned further agrees that the foregoing provisions shall be equally applicable to any issuer-directed shares of Common Stock the undersigned may purchase in the Public Offering.

If the undersigned is an officer or director of the Company, (1) the Representatives agree that, at least three business days before the effective date of any release or waiver of the foregoing restrictions in connection with a transfer of shares of Common Stock, the Representatives will notify the Company of the impending release or waiver, and (2) the Company has agreed in the Underwriting Agreement to announce the impending release or waiver by press release through a major news service at least two business days before the effective date of the release or waiver. Any release or waiver granted by the Representatives hereunder to any such officer or director shall only be effective two business days after the publication date of such press release. The provisions of this paragraph will not apply if (i) the release or waiver is effected solely to permit a transfer not for consideration and (ii) the transferee has agreed in writing to be bound by the same terms described in this lock-up agreement to the extent and for the duration that such terms remain in effect at the time of the transfer.

Notwithstanding the foregoing, and subject to the conditions below, the undersigned may transfer the Lock-Up Securities without the prior written consent of the Representatives as described below, provided that (1) the Representatives receive a signed lock-up agreement for the balance of the Lock-Up Period from each donee, trustee, distributee, or transferee, as the case may be, (2) any such transfer shall not involve a disposition for value, (3) such transfers are not required to be reported with the Securities and Exchange Commission (the "**SEC**") on Form 4 in accordance with Section 16 of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), and (4) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers:

(i) as a *bona fide* gift or gifts; or

(ii) by will or intestacy to the undersigned's legal representative, heir or legatee; or

(iii) by operation of law, such as pursuant to a qualified domestic order or in connection with a divorce settlement; or

(iv) to any trust for the direct or indirect benefit of the undersigned or the immediate family of the undersigned (for purposes of this lock-up agreement, "immediate

family" shall mean any relationship by blood, marriage or adoption, not more remote than first cousin); or

(v) as a distribution to limited partners, limited liability company members or stockholders of the undersigned or other equity holders of the undersigned; or

(vi) to the undersigned's affiliates or to any investment fund or other entity controlled or managed by the undersigned.

Furthermore, the undersigned may:

(i) sell shares of Common Stock of the Company purchased by the undersigned on the open market following the Public Offering if and only if (A) such sales are not required to be reported in any public report or filing with the SEC, or otherwise, and (B) the undersigned does not otherwise voluntarily effect any public filing or report regarding such sales; or

(ii) exercise options to purchase shares of Common Stock granted pursuant to the Company's equity incentive plans by way of cash or "net" or "cashless" exercise, or exchange or convert any Lock-Up Securities convertible or exchangeable for shares of Common Stock, in each case, outstanding as of the date of the final prospectus for this Public Offering and as described therein; *provided* that (A) any exercise or settlement does not involve a transfer of Lock-Up Securities to any person or entity other than the Company, whether to cover the applicable exercise price, withholding tax obligation or otherwise, (B) any shares of Common Stock received upon such exercise, settlement, exchange or conversion shall be subject to all of the restrictions set forth in this lock-up agreement, (C) if required, any public report or filing under Section 16 of the Exchange Act shall clearly indicate in footnotes thereto that such transfer is being made pursuant to the circumstances described in this clause (ii), that no shares were sold by the reporting person and that the shares received upon exercise of the stock option are subject to a lock-up agreement with the underwriters, and (D) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfer that is not otherwise required; or

(iii) transfer Lock-Up Securities (including without limitation, the entering into of any lock-up, voting or similar agreement pursuant to which the undersigned may agree to transfer, sell, tender or otherwise dispose of shares of Common Stock or other securities in connection with such transaction) pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all holders of the Company's share capital involving a Change of Control (as defined below) of the Company that has been approved by the board of directors of the Company; *provided* that (A) all Lock-Up Securities held by the undersigned that are not transferred pursuant to such tender offer, merger, consolidation or other similar transaction shall remain subject to all of the restrictions set forth in this lock-up agreement, (B) in the event that such tender offer, merger, consolidation or other such transaction is not completed, the Lock-Up Securities held by the

undersigned shall remain subject to all of the restrictions set forth in this lock-up agreement, and (C) for purposes of this paragraph, "Change of Control" shall mean the transfer in connection with a consummation of any bona fide third-party tender offer, merger, consolidation or other similar transaction, in one transaction or a series of related transactions, to a "person" (as defined in Section 13(d)(3) of the Exchange Act), or group of persons (other than an underwriter pursuant to the Public Offering), of the Company's voting securities if, the result of which is that person or group of persons, other than the Company, becomes the beneficial owner (as defined in Rules 13d-3 and 13d-5 of the Exchange Act) of 51% of the total voting power of the voting securities of the Company (or the surviving entity); or

(iv) establish a trading plan pursuant to Rule 10b5-1 under the Exchange Act, provided that such plan does not provide for the transfer and sale of shares of Common Stock or any securities convertible into or exercisable or exchangeable for Common Stock during the Lock-Up Period and provided further that no public announcement of the establishment or existence of such plan, and no filing with the SEC, or any other regulatory authority, is required or voluntarily made by or on behalf of the undersigned or the Company in connection with the establishment of such plan.

The undersigned acknowledges and agrees that the underwriters have not provided any recommendation or investment advice nor have the underwriters solicited any action from the undersigned with respect to the offering of the securities and the undersigned has consulted their own legal, accounting, financial, regulatory and tax advisors to the extent deemed appropriate.

The undersigned also agrees and consents to the entry of stop transfer instructions with the Company's transfer agent and registrar against the transfer of the Lock-Up Securities except in compliance with the foregoing restrictions.

This lock-up agreement shall be governed by and construed in accordance with the laws of the State of New York.

[*Signature page follows*]

Very truly yours,

Signature: _____

Name: _____

Exhibit 10.51

Non-employee Director Form

CARIBOU BIOSCIENCES, INC.

2021 EQUITY INCENTIVE PLAN

STOCK OPTION AGREEMENT

Unless otherwise defined herein, the terms defined in the 2021 Equity Incentive Plan (the "Plan") shall have the same defined meanings in this Stock Option Agreement (the "Option Agreement").

I. NOTICE OF STOCK OPTION GRANT

Name: _____

Address: _____

The undersigned (the "Participant") has been granted an Option to purchase Common Stock of the Company, subject to the terms and conditions of the Plan and this Option Agreement, as follows:

Date of Grant:	
Vesting Commencement Date:	
Exercise Price per Share:	$
Total Number of Shares Represented by stock option:	
Total Exercise Price:	$
Type of Option:	Nonqualified Stock Option
Term/Expiration Date:	

Vesting Schedule:

This Option shall be exercisable, in whole or in part, according to the following vesting schedule:

[Vesting schedule], in each case subject to the Participant continuing to be a Non-Employee Director through each such date.

Termination Period:

This Option, to the extent vested, shall be exercisable for three (3) months after Participant ceases to be a Non-Employee Director, unless such termination is due to Participant's death or disability, in which case this Option shall be exercisable for twelve (12) months after Participant ceases to be a Non-Employee Director. Notwithstanding the foregoing sentence, in no event may this Option be exercised after the Term/Expiration Date as provided above and this Option may be subject to earlier termination as provided in Section 14 of the Plan.

II. AGREEMENT

1. Grant of Option. The Administrator hereby grants to the Participant an option (the "Option") to purchase the number of Shares set forth in Section I of this Option Agreement, at the exercise price per Share set forth in Section I of this Option Agreement (the "Exercise Price"), and subject to the terms and conditions of the Plan, which is incorporated herein by reference. Subject to Article 14 of the Plan, in the event of a conflict between the terms and conditions of the Plan and this Option Agreement, the terms and conditions of the Plan shall prevail.

2. Exercise of Option.

(a) Right to Exercise. This Option shall be exercisable during its term in accordance with the Vesting Schedule set forth in Section I of this Option Agreement and with the applicable provisions of the Plan and this Option Agreement.

(b) Method of Exercise. This Option shall be exercisable by delivery of an exercise notice in the form attached as Exhibit A (the "Exercise Notice") or in a manner and pursuant to such procedures as the Administrator may determine, which shall state the election to exercise the Option, the number of Shares with respect to which the Option is being exercised (the "Exercised Shares"), and such other representations and agreements as may be required by the Company. The Exercise Notice shall be accompanied by payment of the aggregate Exercise Price as to all Exercised Shares, together with any applicable tax withholding. This Option shall be deemed to be exercised upon receipt by the Company of such fully executed Exercise Notice accompanied by the aggregate Exercise Price, together with any applicable tax withholding.

No Shares shall be issued pursuant to the exercise of an Option unless such issuance and such exercise comply with Applicable Laws. Assuming such compliance, for income tax purposes the Shares shall be considered transferred to Participant on the date on which the Option is exercised with respect to such Shares.

[Historical Lock-Up: 3. Lock-Up Period. Participant agrees to execute and deliver the lock-up agreement attached hereto as Exhibit B (the "Lock-Up Agreement"). Participant agrees that any transferee of the Option or shares acquired pursuant to the Option shall be bound by this Section 3 and the Lock-Up Agreement.]

4. Method of Payment. Payment of the aggregate Exercise Price shall be by any of the methods permitted in Section 12.1 of the Plan, or a combination thereof, at the election of the Participant and as permitted by the Administrator.

5. Restrictions on Exercise. This Option may not be exercised if the issuance of such Shares upon such exercise or the method of payment of consideration for such shares would constitute a violation of any Applicable Law.

6. Non-Transferability of Option. This Option may not be transferred in any manner otherwise than by will or by the laws of descent or distribution and may be exercised during the lifetime of Participant only by Participant (subject to Section 3 of the Option Agreement). The terms of the Plan and this Option Agreement shall be binding upon the executors, administrators, heirs, successors, and assigns of Participant.

7. Term of Option. This Option may be exercised only within the term set out in Section I of the Option Agreement and may be exercised during such term only in accordance with the Plan and the terms of this Option Agreement. In the event of any transaction or Change in Control (as defined in the Plan), the Option may, in the discretion of the Administrator, be terminated, which may be in exchange for cash or property, be assumed or

substituted by the successor corporation or otherwise continued in full force and effect pursuant to the terms of the Change in Control or other transaction on such terms and conditions as the Administrator determines.

8. Entire Agreement; Governing Law. The Plan is incorporated herein by reference. The Plan and this Option Agreement constitute the entire agreement of the parties with respect to the subject matter hereof and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof, and may not be modified adversely to the Participant's interest except by means of a writing signed by the Company and Participant. This Option Agreement is governed by the internal substantive laws but not the choice of law rules of Delaware.

9. No Guarantee of Continued Service. PARTICIPANT ACKNOWLEDGES AND AGREES THAT THE VESTING OF SHARES PURSUANT TO THE VESTING SCHEDULE HEREOF IS EARNED ONLY BY CONTINUING AS A NON-EMPLOYEE DIRECTOR AT THE WILL OF THE COMPANY (OR THE PARENT OR SUBSIDIARY EMPLOYING OR RETAINING PARTICIPANT) AND NOT THROUGH THE ACT OF BEING HIRED, BEING GRANTED THIS OPTION, OR ACQUIRING SHARES HEREUNDER. PARTICIPANT FURTHER ACKNOWLEDGES AND AGREES THAT THIS AGREEMENT, THE TRANSACTIONS CONTEMPLATED HEREUNDER, AND THE VESTING SCHEDULE SET FORTH HEREIN DO NOT CONSTITUTE AN EXPRESS OR IMPLIED PROMISE OF CONTINUED ENGAGEMENT AS A NON-EMPLOYEE DIRECTOR FOR THE VESTING PERIOD, FOR ANY PERIOD, OR AT ALL, AND SHALL NOT INTERFERE IN ANY WAY WITH PARTICIPANT'S RIGHT OR THE RIGHT OF THE COMPANY (OR THE PARENT OR SUBSIDIARY EMPLOYING OR RETAINING PARTICIPANT) OR THE COMPANY'S SHAREHOLDERS TO TERMINATE PARTICIPANT'S RELATIONSHIP AS A NON-EMPLOYEE DIRECTOR AT ANY TIME, WITH OR WITHOUT CAUSE OR TO ELECT AND REMOVE DIRECTORS.

Participant acknowledges receipt of a copy of the Plan and represents that they are familiar with the terms and provisions thereof, and hereby accepts this Option subject to all of the terms and provisions thereof. Participant has reviewed the Plan and this Option in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Option, and fully understands all provisions of the Option. Participant hereby agrees to accept as binding, conclusive, and final all decisions or interpretations of the Administrator upon any questions arising under the Plan or this Option. Participant further agrees to notify the Company upon any change in the residence address indicated below.

PARTICIPANT	CARIBOU BIOSCIENCES, INC.
Signature	By
Print Name	Print Name
Residence Address	Title

EXHIBIT A

2021 EQUITY INCENTIVE PLAN

EXERCISE NOTICE

Caribou Biosciences, Inc.
2929 7th Street, Suite 105
Berkeley, CA 94710

Attention: President

1. Exercise of Option. Effective as of today, _____ , _____ , the undersigned ("Participant") hereby elects to exercise Participant's option (the "Option") to purchase _____ shares of the Common Stock (the "Shares") of Caribou Biosciences, Inc. (the "Company") under and pursuant to the 2021 Equity Incentive Plan (the "Plan") and the Stock Option Agreement dated _____ ,_____(the "Option Agreement").

2. Delivery of Payment. Participant herewith delivers to the Company the full purchase price of the Shares, as set forth in the Option Agreement, and any and all withholding taxes due in connection with the exercise of the Option using a method provided in Section 12.1 of the Plan as may be permitted by the Administrator.

3. Representations of Participant. Participant acknowledges that Participant has received, read, and understood the Plan and the Option Agreement and agrees to abide by and be bound by their terms and conditions.

4. Rights as Stockholder. Until the issuance of the Shares (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company), no right to vote or receive dividends or any other rights as a stockholder shall exist with respect to the Common Stock subject to an Award, notwithstanding the exercise of the Option. The Shares shall be issued to Participant as soon as practicable after the Option is exercised in accordance with the Option Agreement. No adjustment shall be made for a dividend or other right for which the record date is prior to the date of issuance except as provided in Section 14 of the Plan.

5. Tax Consultation. Participant understands that Participant may suffer adverse tax consequences as a result of Participant's purchase or disposition of the Shares. Participant represents that Participant has consulted with any tax consultants Participant deems advisable in connection with the purchase or disposition of the Shares and that Participant is not relying on the Company for any tax advice.

6. Successors and Assigns. The Company may assign any of its rights under this Exercise Notice to single or multiple assignees, and this Exercise Notice shall inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer herein set forth, this Exercise Notice shall be binding upon Participant and their heirs, executors, administrators, successors and assigns.

7. Interpretation. Any dispute regarding the interpretation of this Exercise Notice shall be submitted by Participant or by the Company forthwith to the Administrator, which shall review such dispute at its next regular meeting. The resolution of such a dispute by the Administrator shall be final and binding on all parties.

8. Governing Law; Severability. This Exercise Notice is governed by the internal substantive laws, but not the choice of law rules, of Delaware. In the event that any provision hereof becomes or is declared by a court of competent jurisdiction to be illegal, unenforceable, or void, this Exercise Notice shall continue in full force and effect.

9. Entire Agreement. The Plan and Option Agreement are incorporated herein by reference. This Exercise Notice, the Plan, and the Option Agreement constitute the entire agreement of the parties with respect to the subject matter hereof and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof, and may not be modified adversely to the Participant's interest except by means of a writing signed by the Company and Participant.

Submitted by:	Accepted by:
PARTICIPANT	CARIBOU BIOSCIENCES, INC.
	By: _____
_____	
Signature	
_____	_____
Print Name	Print Name
Address:	_____
	Title
_____	
_____	Address:
_____	2929 7th Street, Suite 105 Berkeley, CA 94710
	_____
	Date Received

[EXHIBIT B

_____, 2021

BofA Securities, Inc.
Citigroup Global Markets Inc.
SVB Leerink LLC

as Representatives of the several
Underwriters to be named in the
within-mentioned Underwriting Agreement

c/o BofA Securities, Inc.
One Bryant Park
New York, New York 10036

Citigroup Global Markets Inc.
388 Greenwich Street
New York, New York 10013

SVB Leerink LLC
One Federal Street, 37th Floor
Boston, Massachusetts 02110

Re: Proposed Public Offering by Caribou Biosciences, Inc.

Dear Ladies and Gentlemen:

The undersigned, a stockholder and/or a stock option holder and/or an officer and/or a director, as applicable, of Caribou Biosciences, Inc., a Delaware corporation (the "**Company**"), understands that BofA Securities, Inc., Citigroup Global Markets Inc. and SVB Leerink LLC (collectively, the "**Representatives**") previously entered into an Underwriting Agreement, dated July 22, 2021 (the "**Underwriting Agreement**") with the Company and the other underwriters party thereto providing for the public offering (the "**Public Offering**") of shares of the Company's common stock, par value $0.0001 per share (the "**Common Stock**"). In recognition of the benefit that the Public Offering has conferred upon the undersigned as a stockholder and/or a stock option holder and/or an officer and/or a director, as applicable, of the Company, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the undersigned agrees with each underwriter named in the Underwriting Agreement that, during the period beginning on the date hereof and ending on the date that is 180 days from the date of the Underwriting Agreement (the "**Lock-Up Period**"), the undersigned will not, without the prior written consent of the Representatives, (i) directly or indirectly, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or

contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of any shares of the Company's Common Stock or any securities convertible into or exercisable or exchangeable for shares of Common Stock, whether now owned or hereafter acquired by the undersigned or with respect to which the undersigned has or hereafter acquires the power of disposition (collectively, the "**Lock-Up Securities**"), or exercise any right with respect to the registration of any of the Lock-Up Securities, or file, cause to be filed or cause to be confidentially submitted any registration statement in connection therewith, under the Securities Act of 1933, as amended, (ii) enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of the Lock-Up Securities, whether any such swap or transaction is to be settled by delivery of shares of Common Stock or other securities, in cash or otherwise or (iii) publicly disclose the intention to do any of the foregoing described in clauses (i) and (ii) above. If the undersigned is an officer or director of the Company, the undersigned further agrees that the foregoing provisions shall be equally applicable to any issuer-directed shares of Common Stock the undersigned may purchase in the Public Offering.

If the undersigned is an officer or director of the Company, (1) the Representatives agree that, at least three business days before the effective date of any release or waiver of the foregoing restrictions in connection with a transfer of shares of Common Stock, the Representatives will notify the Company of the impending release or waiver, and (2) the Company has agreed in the Underwriting Agreement to announce the impending release or waiver by press release through a major news service at least two business days before the effective date of the release or waiver. Any release or waiver granted by the Representatives hereunder to any such officer or director shall only be effective two business days after the publication date of such press release. The provisions of this paragraph will not apply if (i) the release or waiver is effected solely to permit a transfer not for consideration and (ii) the transferee has agreed in writing to be bound by the same terms described in this lock-up agreement to the extent and for the duration that such terms remain in effect at the time of the transfer.

Notwithstanding the foregoing, and subject to the conditions below, the undersigned may transfer the Lock-Up Securities without the prior written consent of the Representatives as described below, provided that (1) the Representatives receive a signed lock-up agreement for the balance of the Lock-Up Period from each donee, trustee, distributee, or transferee, as the case may be, (2) any such transfer shall not involve a disposition for value, (3) such transfers are not required to be reported with the Securities and Exchange Commission (the "**SEC**") on Form 4 in accordance with Section 16 of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), and (4) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers:

(i) as a *bona fide* gift or gifts; or

(ii) by will or intestacy to the undersigned's legal representative, heir or legatee; or

(iii) by operation of law, such as pursuant to a qualified domestic order or in connection with a divorce settlement; or

(iv) to any trust for the direct or indirect benefit of the undersigned or the immediate family of the undersigned (for purposes of this lock-up agreement, "immediate family" shall mean any relationship by blood, marriage or adoption, not more remote than first cousin); or

(v) as a distribution to limited partners, limited liability company members or stockholders of the undersigned or other equity holders of the undersigned; or

(vi) to the undersigned's affiliates or to any investment fund or other entity controlled or managed by the undersigned.

Furthermore, the undersigned may:

(i) sell shares of Common Stock of the Company purchased by the undersigned on the open market following the Public Offering if and only if (A) such sales are not required to be reported in any public report or filing with the SEC, or otherwise, and (B) the undersigned does not otherwise voluntarily effect any public filing or report regarding such sales; or

(ii) exercise options to purchase shares of Common Stock granted pursuant to the Company's equity incentive plans by way of cash or "net" or "cashless" exercise, or exchange or convert any Lock-Up Securities convertible or exchangeable for shares of Common Stock, in each case, outstanding as of the date of the final prospectus for this Public Offering and as described therein; *provided* that (A) any exercise or settlement does not involve a transfer of Lock-Up Securities to any person or entity other than the Company, whether to cover the applicable exercise price, withholding tax obligation or otherwise, (B) any shares of Common Stock received upon such exercise, settlement, exchange or conversion shall be subject to all of the restrictions set forth in this lock-up agreement, (C) if required, any public report or filing under Section 16 of the Exchange Act shall clearly indicate in footnotes thereto that such transfer is being made pursuant to the circumstances described in this clause (ii), that no shares were sold by the reporting person and any securities convertible into or exercisable or exchangeable for Common Stock during the Lock-Up Period and provided further that no public announcement of the establishment or existence of such plan, and no filing with the SEC, or any other regulatory authority, is required or voluntarily made by or on behalf of the undersigned or the Company in connection with the establishment of such plan.

The undersigned acknowledges and agrees that the underwriters have not provided any recommendation or investment advice nor have the underwriters solicited any action from the undersigned with respect to the offering of the securities and the undersigned has consulted their own legal, accounting, financial, regulatory and tax advisors to the extent deemed appropriate.

The undersigned also agrees and consents to the entry of stop transfer instructions with the Company's transfer agent and registrar against the transfer of the Lock-Up Securities except in compliance with the foregoing restrictions.

This lock-up agreement shall be governed by and construed in accordance with the laws of the State of New York.]

[*Signature page follows*]

Very truly yours,

Signature: _____

Name: _____

CARIBOU BIOSCIENCES, INC.
2021 EQUITY INCENTIVE PLAN

RESTRICTED STOCK UNIT AWARD GRANT NOTICE

Caribou Biosciences, Inc., a Delaware corporation (the "Company"), pursuant to its 2021 Equity Incentive Plan (the "Plan"), hereby grants to the holder listed below (the "Participant"), an award of restricted stock units ("Restricted Stock Units" or "RSUs"). Each vested Restricted Stock Unit represents the right to receive, in accordance with the Restricted Stock Unit Award Agreement attached hereto as Exhibit A (the "Agreement"), one share of Common Stock ("Share"). This award of Restricted Stock Units is subject to all of the terms and conditions set forth herein and in the Agreement and the Plan, each of which are incorporated herein by reference. Unless otherwise defined herein, the terms defined in the Plan shall have the same defined meanings in this Restricted Stock Unit Award Grant Notice (the "Grant Notice") and the Agreement.

Participant:	%%FIRST_NAME_MIDDLE_NAME_LAST_NAME%-%
Grant Date:	%AWARD_DATE,'Month DD, YYYY'%-%
Total Number of RSUs:	%%TOTAL_SHARES_GRANTED,'999,999,999'%-%
Vesting Commencement Date:	%%VEST_BASE_DATE,'Month DD, YYYY'%-%
Vesting Schedule:	Twenty-five percent (25%) of the Shares subject to the RSU shall vest on each of the one (1), two (2), three (3), and four (4) year anniversaries of the Vesting Commencement Date, subject to Participant continuing to be an Employee through each such date. On each vesting date, the number of Shares vesting shall be rounded down to the nearest whole share, with the balance vesting on the last vesting date.
Termination:	If the Participant experiences a Termination of Service, all RSUs that have not become vested on or prior to the date of such Termination of Service will thereupon be automatically forfeited by the Participant without payment of any consideration therefor.

By their signature and the Company's signature below, the Participant agrees to be bound by the terms and conditions of the Plan, the Agreement and this Grant Notice. The Participant has reviewed the Agreement, the Plan and this Grant Notice in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Grant Notice and fully understands all provisions of this Grant Notice, the Agreement, and the Plan. The Participant hereby agrees to accept as binding, conclusive, and final all decisions or interpretations of the Administrator upon any questions arising under the Plan, this Grant Notice, or the Agreement. In addition, by signing below, the Participant also agrees that the Company, in its sole discretion, may satisfy any withholding obligations in accordance with Section 2.6(b) of the Agreement by (i) withholding shares of Common Stock otherwise issuable to the Participant upon vesting of the RSUs, (ii) instructing a broker on the Participant's behalf to sell shares of Common Stock otherwise issuable to the Participant upon vesting of the RSUs and submit the proceeds of such sale to the Company, or (iii) using any other method permitted by Section 2.6(b) of the Agreement or the Plan.

PARTICIPANT	CARIBOU BIOSCIENCES, INC.
Signature	By
%%FIRST_NAME_MIDDLE_NAME_LAST_NAME%-%	/s/ Rachel E. Haurwitz
Print Name %%ADDRESS_LINE_1%-% %%ADDRESS_LINE_2%-% %%ADDRESS_LINE_3%-% %%COUNTRY%-% Residence Address	Print Name: Rachel E. Haurwitz, Ph.D. Title: President & CEO

EXHIBIT A
TO RESTRICTED STOCK UNIT AWARD GRANT NOTICE

RESTRICTED STOCK UNIT AWARD AGREEMENT

Pursuant to the Restricted Stock Unit Award Grant Notice (the "Grant Notice") to which this Restricted Stock Unit Award Agreement (this "Agreement") is attached, Caribou Biosciences, Inc., a Delaware corporation (the "Company"), has granted to the Participant the number of restricted stock units ("Restricted Stock Units" or "RSUs") set forth in the Grant Notice under the Company's 2021 Equity Incentive Plan (the "Plan"). Each Restricted Stock Unit represents the right to receive one share of Common Stock (a "Share") upon vesting. Capitalized terms not specifically defined herein shall have the meanings specified in the Plan and Grant Notice.

ARTICLE I
GENERAL

1.1 Incorporation of Terms of Plan. The RSUs are subject to the terms and conditions of the Plan, which are incorporated herein by reference. In the event of any inconsistency between the Plan and this Agreement, the terms of the Plan shall control.

ARTICLE II
GRANT OF RESTRICTED STOCK UNITS

2.1 Grant of RSUs. Pursuant to the Grant Notice and upon the terms and conditions set forth in the Plan and this Agreement, effective as of the Grant Date set forth in the Grant Notice, the Company hereby grants to the Participant an award of RSUs under the Plan in consideration of the Participant's past and/or continued employment with or service to the Company or any Subsidiaries and for other good and valuable consideration.

2.2 Unsecured Obligation to RSUs. Unless and until the RSUs have vested in the manner set forth in Article 2 hereof, the Participant will have no right to receive Common Stock under any such RSUs. Prior to actual payment of any vested RSUs, such RSUs will represent an unsecured obligation of the Company, payable (if at all) only from the general assets of the Company.

2.3 Vesting Schedule. Subject to Section 2.5 hereof, the RSUs shall vest and become nonforfeitable with respect to the applicable portion thereof according to the vesting schedule set forth in the Grant Notice (rounding down to the nearest whole Share). Except as may otherwise be provided in any employment agreement, in the event of any transaction or Change in Control (as defined in the Plan), the RSUs may, in the discretion of the Administrator, be terminated, which may be in exchange for cash or property, be assumed or substituted by the successor corporation or otherwise continued in full force and effect pursuant to the terms of the Change in Control or other transaction on such terms and conditions as the Administrator determines.

2.4 Consideration to the Company. In consideration of the grant of the award of RSUs pursuant hereto, the Participant agrees to render faithful and efficient services to the Company or any Subsidiary.

2.5 Forfeiture, Termination and Cancellation upon Termination of Service. Notwithstanding any contrary provision of this Agreement or the Plan, upon the Participant's Termination of Service for any or no reason, all Restricted Stock Units which have not vested prior to or in connection with such Termination of Service shall thereupon automatically be forfeited, terminated and cancelled as of the applicable termination date without payment of any consideration by the Company, and the Participant, or the Participant's beneficiary or personal representative, as the case may be, shall have no further rights hereunder. No portion of the RSUs which has not become vested as of the date on which the Participant incurs a Termination of Service shall thereafter become vested.

2.6 Issuance of Common Stock upon Vesting.

(a) As soon as administratively practicable following the vesting of any Restricted Stock Units pursuant to Section 2.3 hereof, but in no event later than thirty (30) days after such vesting date (for the avoidance of doubt, this deadline is intended to comply with the "short term deferral" exemption from Section 409A of the Code), the Company shall deliver to the Participant (or any transferee permitted under Section 3.2 hereof) a number of Shares equal to the number of RSUs subject to this Award that vest on the applicable vesting date.

(b) As set forth in Section 12.2 of the Plan, the Company shall have the authority and the right to deduct or withhold, or to require the Participant to remit to the Company, an amount sufficient to satisfy all applicable federal, state and local taxes required by law to be withheld with respect to any taxable event arising in connection with the Restricted Stock Units. The Company shall not be obligated to deliver any Shares to the Participant or the Participant's legal representative unless and until the Participant or the Participant's legal representative shall have paid or otherwise satisfied in full the amount of all federal, state and local taxes applicable to the taxable income of the Participant resulting from the grant or vesting of the Restricted Stock Units or the issuance of Shares.

2.7 Conditions to Delivery of Shares. The Shares deliverable hereunder may be either previously authorized but unissued Shares, treasury Shares or issued Shares which have then been reacquired by the Company. Such Shares shall be fully paid and nonassessable. The Company shall not be required to issue Shares deliverable hereunder prior to fulfillment of the conditions set forth in Section 12.4 of the Plan.

2.8 Rights as Stockholder. The holder of the RSUs shall not be, nor have any of the rights or privileges of, a stockholder of the Company, including, without limitation, voting rights and rights to dividends, in respect of the RSUs and any Shares underlying the RSUs and deliverable hereunder unless and until such Shares shall have been issued by the Company and held of record by such holder (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company). No adjustment shall be made for a dividend or other right for which the record date is prior to the date the Shares are issued, except as provided in Section 14.2 of the Plan.

ARTICLE III
OTHER PROVISIONS

3.1 Administration. The Administrator shall have the power to interpret the Plan and this Agreement and to adopt such rules for the administration, interpretation and application of the Plan as are consistent therewith and to interpret, amend or revoke any such rules. All actions taken and all interpretations and determinations made by the Administrator in good faith shall be final and binding upon the Participant, the Company and all other interested persons. No member of the Administrator or the Board shall be personally liable for any action, determination or interpretation made in good faith with respect to the Plan, this Agreement or the RSUs.

3.2 RSUs Not Transferable. The RSUs shall be subject to the restrictions on transferability set forth in Section 12.3 of the Plan.

3.3 Tax Consultation. The Participant understands that the Participant may suffer adverse tax consequences in connection with the RSUs granted pursuant to this Agreement (and the Shares issuable with respect thereto). The Participant represents that the Participant has consulted with any tax consultants the Participant deems advisable in connection with the RSUs and the issuance of Shares with respect thereto and that the Participant is not relying on the Company for any tax advice.

3.4 Binding Agreement. Subject to the limitation on the transferability of the RSUs contained herein, this Agreement will be binding upon and inure to the benefit of the heirs, legatees, legal representatives, successors and assigns of the parties hereto.

3.5 Adjustments Upon Specified Events. The Administrator may accelerate the vesting of the RSUs in such circumstances as it, in its sole discretion, may determine. The Participant acknowledges that the RSUs are subject to adjustment, modification and termination in certain events as provided in this Agreement and Section 14.2 of the Plan.

3.6 Notices. Any notice to be given under the terms of this Agreement to the Company shall be addressed to the Company in care of the Secretary of the Company at the Company's principal office, and any notice to be given to the Participant shall be addressed to the Participant at the Participant's last address reflected on the Company's records. By a notice given pursuant to this Section 3.6, either party may hereafter designate a different address for notices to be given to that party. Any notice shall be deemed duly given when sent via email or when sent by certified mail (return receipt requested) and deposited (with postage prepaid) in a post office or branch post office regularly maintained by the United States Postal Service.

3.7 Participant's Representations. If the Shares issuable hereunder have not been registered under the Securities Act or any applicable state laws on an effective registration statement at the time of such issuance, the Participant shall, if required by the Company, concurrently with such issuance, make such written representations as are deemed necessary or appropriate by the Company and/or its counsel.

3.8 Titles. Titles are provided herein for convenience only and are not to serve as a basis for interpretation or construction of this Agreement.

3.9 Governing Law. The laws of the State of Delaware shall govern the interpretation, validity, administration, enforcement and performance of the terms of this Agreement regardless of the law that might be applied under principles of conflicts of laws.

3.10 Conformity to Securities Laws. The Participant acknowledges that the Plan and this Agreement are intended to conform to the extent necessary with all provisions of the Securities Act and the Exchange Act and any other Applicable Law. Notwithstanding anything herein to the contrary, the Plan shall be administered, and the RSUs are granted, only in such a manner as to conform to Applicable Law. To the extent permitted by Applicable Law, the Plan and this Agreement shall be deemed amended to the extent necessary to conform to such Applicable Law.

3.11 Amendment, Suspension and Termination. To the extent permitted by the Plan, this Agreement may be wholly or partially amended or otherwise modified, suspended or terminated at any time or from time to time by the Administrator or the Board; *provided, however,* that, except as may otherwise be provided by the Plan, no amendment, modification, suspension or termination of this Agreement shall adversely affect the RSUs in any material way without the prior written consent of the Participant.

3.12 Successors and Assigns. The Company may assign any of its rights under this Agreement to single or multiple assignees, and this Agreement shall inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer herein set forth in Section 3.2 hereof, this Agreement shall be binding upon the Participant and their heirs, executors, administrators, successors, and assigns.

3.13 Limitations Applicable to Section 16 Persons. Notwithstanding any other provision of the Plan or this Agreement, if the Participant is subject to Section 16 of the Exchange Act, then the Plan, the RSUs, and this

Agreement shall be subject to any additional limitations set forth in any applicable exemptive rule under Section 16 of the Exchange Act (including any amendment to Rule 16b-3 of the Exchange Act) that are requirements for the application of such exemptive rule. To the extent permitted by Applicable Law, this Agreement shall be deemed amended to the extent necessary to conform to such applicable exemptive rule.

3.14 Not a Contract of Service Relationship. Nothing in this Agreement or in the Plan shall confer upon Participant any right to continue to serve as an employee or other service provider of the Company or any of its Subsidiaries or interfere with or restrict in any way with the right of the Company or any of its Subsidiaries, which rights are hereby expressly reserved, to discharge or to terminate for any reason whatsoever, with or without cause, the services of the Participant's at any time.

3.15 Entire Agreement. The Plan, the Grant Notice, and this Agreement (including all Exhibits thereto, if any) constitute the entire agreement of the parties and supersede in their entirety all prior undertakings and agreements of the Company and the Participant with respect to the subject matter hereof.

3.16 Section 409A. This Award is not intended to constitute "nonqualified deferred compensation" within the meaning of Section 409A of the Code (together with any Department of Treasury regulations and other interpretive guidance issued thereunder, including without limitation any such regulations or other guidance that may be issued after the date hereof, "Section 409A"). However, notwithstanding any other provision of the Plan, the Grant Notice or this Agreement, if at any time the Administrator determines that this Award (or any portion thereof) may be subject to Section 409A, the Administrator shall have the right in its sole discretion (without any obligation to do so or to indemnify Participant or any other person for failure to do so) to adopt such amendments to the Plan, the Grant Notice or this Agreement, or adopt other policies and procedures (including amendments, policies and procedures with retroactive effect), or take any other actions, as the Administrator determines are necessary or appropriate for this Award either to be exempt from the application of Section 409A or to comply with the requirements of Section 409A.

3.17 Limitation on Participant's Rights. Participation in the Plan confers no rights or interests other than as herein provided. This Agreement creates only a contractual obligation on the part of the Company as to amounts payable and shall not be construed as creating a trust. Neither the Plan nor any underlying program, in and of itself, has any assets. The Participant shall have only the rights of a general unsecured creditor of the Company and its Subsidiaries with respect to amounts credited and benefits payable, if any, with respect to the RSUs, and rights no greater than the right to receive the Common Stock as a general unsecured creditor with respect to RSUs, as and when payable hereunder.

Exhibit 21.1

Subsidiaries of Caribou Biosciences, Inc.

Entity	State or Jurisdiction of Incorporation or Organization
Antler Holdco, LLC	Delaware
Arboreal Holdco, LLC	Delaware
Biloba Holdco, LLC	Delaware
Microbe Holdco, LLC	Delaware

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-258173 on Form S-8 of our report dated March 21, 2022, relating to the financial statements of Caribou Biosciences, Inc., appearing in this Annual Report on Form 10-K of Caribou Biosciences, Inc. for the year ended December 31, 2021.

/s/ Deloitte & Touche
San Francisco, California
March 21, 2022

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Rachel E. Haurwitz, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2021 of Caribou Biosciences, 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)) 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) 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

   (c) 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 21, 2022

By: /s/ Rachel E. Haurwitz
Rachel E. Haurwitz
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Jason V. O'Byrne, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2021 of Caribou Biosciences, 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 officers 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)) 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) 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

   (c) 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 officers 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 21, 2022

By: /s/ Jason V. O'Byrne

Jason V. O'Byrne
Chief Financial Officer

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Caribou Biosciences, Inc. (the "Company") on Form 10-K for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 21, 2022

By: /s/ Rachel E. Haurwitz
Rachel E. Haurwitz
President and Chief Executive Officer

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Caribou Biosciences, Inc. (the "Company") on Form 10-K for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 21, 2022

By: /s/ Jason V. O'Byrne

Jason V. O'Byrne
Chief Financial Officer