PRECISION BIOSCIENCES

Fiscal Year 2019 Annual Report

Dedicated to IMPROVING LIFE

To our stockholders,

It's a great pleasure to be writing to you at the end of our first year as a public company, after what was a remarkable 2019 for Precision BioSciences. We started the year as a privately held, preclinical stage company with an extraordinary gene editing technology platform developed by our founders and team, but without clinical validation of our science. Fast forward 12 months, and Precision has completed a successful Nasdaq IPO, advanced three novel off-the-shelf, or allogeneic, CAR T cell therapies into clinical development, demonstrated that our science has the potential to treat cancers in patients with few other options, built and opened a first-in-class manufacturing facility, broken new ground in the development of *in vivo* gene correction therapies, created a state-of-the-art independent new home for Elo Life Systems, and expanded our team of Precisioneers to more than 200 talented and passionate people.

It's an extraordinary pace of progress and growth, and one that makes me proud to be a part of this incredible team.

Dedicated To Improving Life

We say this often, but at Precision we really are **d**edicated **t**o **i**mproving **l**ife – it's even in our stock ticker, DTIL. I sometimes get asked what this means – put simply, this is the core of our approach to everything we do.

We firmly believe that, with our ARCUS platform, we have developed the best gene editing technology that exists today. ARCUS is unique in the editing world. Through a lot of hard work and complex protein engineering, we were able to develop ARCUS from an enzyme found naturally in algae, which evolved specifically to perform very precise genetic edits. ARCUS is versatile, small and easy to package for delivery, and has a natural "off-switch" built in. We think this profile makes ARCUS enormously compelling for use in medicine and other applications.

But that in itself isn't enough – our mission is to take this platform and use it to significantly improve human health and wellness across multiple facets of life. And also, importantly, to do our part through scientific innovation to reduce the overall cost burden of healthcare on society. It's an ambitious goal, but it's one that drives every single person at Precision. Today, we are focused on three important areas – fighting cancer, using gene editing to cure rare and infectious diseases, and improving human food sources. We believe we can make an important difference to the lives of millions of people and we strive every day to make this belief a reality.

Leading the way in allogeneic CAR T

The progress we made in 2019 in the first of these areas, our off-the-shelf CAR T immunotherapy portfolio for the treatment of cancer, is particularly exciting. Cell therapy for cancer is one of the true breakthroughs of modern medicine and the approved autologous CAR T products that are already on the market have had an incredible positive impact on the lives of many cancer patients. But there are still limitations to this approach, not least in terms of access to treatment, cost and safety considerations.

At Precision, we have believed for some time that many of the unique features of ARCUS could allow us to develop a truly off-the-shelf CAR T therapy – one that can deliver the incredible potency of CAR T, but which could sit on a shelf just like any other drug and be used quickly, and safely, when a patient needs it. That dream came a step closer to reality in 2019 when we were able to present initial clinical data from our CD19-targeting PBCAR0191 Phase 1/2a clinical trial treating patients with non-Hodgkin lymphoma (NHL) and acute lymphoblastic leukemia (ALL). Those data demonstrated that an off-the-shelf CAR T therapy can shrink patients' cancers with very few side effects and without first needing harsh and complex conditioning steps. This was a landmark moment for Precision and, we think, the whole allogeneic CAR T field, and I believe begins to validate our approach in this area.

We are pushing forward fast with this trial, but we aren't stopping there. We are excited also to be starting two further CAR T trials in 2020, one with our CD20-targeting PBCAR20A, also for patients with NHL as well as chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL), and our BCMA-targeting PBCAR269A for patients with multiple myeloma. The last of these will be the first of our trials to produce CAR T cells in-house at our newly opened Manufacturing Center for Advanced Therapeutics (MCAT). It's another great testament to what Precision achieved in 2019 that we were able to successfully construct,

test and open this facility, which we believe is a powerful strategic asset for our company. MCAT gives us tremendous control of all the key components of our CAR T therapies, and in the future also our *in vivo* gene therapies, and means we are no longer reliant solely on third parties to bring our therapies to patients. We are very excited to continue to update you on our progress in CAR T throughout 2020.

A portfolio with depth and breadth

While CAR T is a key focus for Precision right now, our portfolio extends well beyond this arena. In 2019 we made solid progress with our *in vivo* gene correction pipeline, which is focused on using ARCUS to directly and permanently overcome genetic and infectious diseases within the body. We believe this is ultimately the area where the unique safety profile, versatility and ease of delivery of ARCUS are the most important, and will allow us to take a true leadership position.

In this area, we are making good progress on a potential gene editing-based cure for chronic hepatitis B. We also advanced our wholly owned gene correction portfolio during 2019, and I was pleased to announce recently that we have selected as our lead, a program targeting the rare genetic disease primary hyperoxaluria type 1 (PH1). PH1 is a terrible disease, affecting adults and children, and often the only treatment option is to undergo a combined liver-kidney transplant. Based on a compelling set of preclinical data that we generated in partnership with Jim Wilson at U. Penn, we believe that we can develop an ARCUS-based treatment that, with a single administration, can cure patients for life. We are still early in our work here, but we are moving forward fast.

Perhaps the most overlooked part of the Precision vision is our food and agriculture subsidiary Elo Life Systems, which is focused on harnessing ARCUS and other technologies to help combat the effects of climate change on our global food supply and to develop healthier and more sustainable sources of nutrition. I am personally really thrilled by what the Elo team has achieved in 2019, not least in being the first group ever to demonstrate the ability to reactivate dormant genes in a plant, in our ZeroMelon™ zero calorie watermelon sweetener program.

Delivering on the promise of gene editing for patients and consumers worldwide

Derek Jantz, Jeff Smith and I founded Precision 14 years ago. It has been a long journey already, and one that hasn't always been easy, but we start 2020 stronger than we have ever been before. This is just the beginning of a path that the whole team knows will see us bringing truly revolutionary medicines and products to patients in need, and to consumers looking for better health and wellness. We all recognize the duty we have as stewards of a unique and powerful technology that has the potential to do an enormous amount of good for millions of people around the world.
Our deepest thanks go to all our patients, clinicians, partners, communities, Precisioneers and you, our shareholders. We have come a long way, and we couldn't do it without you. Here's to another transformational year in 2020!

Yours,

Matt Kane
Co-founder & CEO

PRECISION BIOSCIENCES

Safe Harbor Statement

Statements in this letter regarding the Company's planned strategy, business focus and intended product development, are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements speak only as of the date such statements are made and are subject to risks and uncertainties that could cause the Company's results to differ materially from these statements. These risks and uncertainties are described in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 under the caption "Risk Factors," as such factors may be updated from time to time in the Company's other filings with the SEC. All forward-looking statements speak only as of the date of this letter and, except as required by applicable law, the Company does plan to publicly update or revise any such forward-looking statements, whether as a result of any new information, future events, changed circumstances or otherwise.

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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2019
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 001-38841

Precision BioSciences, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**20-4206017**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
302 East Pettigrew St., Suite A-100 Durham, North Carolina	**27701**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (919) 314-5512

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 $0.000005 per share	DTIL	The Nasdaq Global Select Market

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

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

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

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

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

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

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

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

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

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 June 28, 2019, was $589.0 million.

The number of shares of Registrant's common stock outstanding as of March 2, 2020 was 51,399,847.

DOCUMENTS INCORPORATED BY REFERENCE

None.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of present and historical facts contained in this Annual Report on Form 10-K, including without limitation, statements regarding our future results of operations and financial position, business strategy and approach, including related results, prospective products, planned preclinical or greenhouse studies and clinical or field trials, the status and results of our preclinical and clinical studies, expected release of interim data, expectations regarding our allogeneic chimeric antigen receptor T cell immunotherapy product candidates, capabilities of our manufacturing facility, regulatory approvals, research and development costs, timing, expected results and likelihood of success, as well as plans and objectives of management for future operations, may be forward-looking statements. Without limiting the foregoing, 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," "seeks," or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. No forward-looking statement is a guarantee of future results, performance, or achievements, and one should avoid placing undue reliance on such statements.

Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to us. Such beliefs and assumptions may or may not prove to be correct. Additionally, such forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those identified in Part I. Item 1A. "Risk Factors" and Part II. Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations." These risks and uncertainties include, but are not limited to:

- our ability to become profitable;
- our ability to procure sufficient funding and requirements under our current debt instruments;
- our operating expenses and our ability to predict what those expenses will be;
- our limited operating history;
- the success of our programs and product candidates in which we expend our resources;
- our dependence on our ARCUS technology;
- the initiation, cost, timing, progress, achievement of milestones and results of research and development activities, preclinical or greenhouse studies and clinical or field trials;
- public perception about genome editing technology and its applications;
- competition in the genome editing, biopharmaceutical, biotechnology and agricultural biotechnology fields;
- our or our collaborators' ability to identify, develop and commercialize product candidates;
- pending and potential liability lawsuits and penalties against us or our collaborators related to our technology and our product candidates;
- the U.S. and foreign regulatory landscape applicable to our and our collaborators' development of product candidates;
- our or our collaborators' ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate;
- our or our collaborators' ability to advance product candidates into, and successfully design, implement and complete, clinical or field trials;
- potential manufacturing problems associated with the development or commercialization of any of our product candidates;
- our ability to achieve our anticipated operating efficiencies at our manufacturing facility;
- delays or difficulties in our and our collaborators' ability to enroll patients;
- if our product candidates do not work as intended or cause undesirable side effects;
- risks associated with applicable healthcare, data privacy and security regulations and our compliance therewith;
- the rate and degree of market acceptance of any of our product candidates;

- the success of our existing collaboration agreements, and our ability to enter into new collaboration arrangements;
- our current and future relationships with third parties including suppliers and manufacturers;
- our ability to obtain and maintain intellectual property protection for our technology and any of our product candidates;
- potential litigation relating to infringement or misappropriation of intellectual property rights;
- our ability to effectively manage the growth of our operations;
- our ability to attract, retain, and motivate key scientific and management personnel;
- market and economic conditions;
- effects of natural and manmade disasters;
- insurance expenses and exposure to uninsured liabilities; and
- fluctuations in our stock price.

Moreover, we operate in an 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.

You should read this Annual Report on Form 10-K and the documents that we reference herein completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements. All forward-looking statements contained herein speak only as of the date of this Annual Report on Form 10-K. 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.

As used in this Annual Report on Form 10-K, unless otherwise stated or the context requires otherwise, references to "Precision," the "Company," "we," "us," and "our," refer to Precision BioSciences, Inc. and its subsidiaries on a consolidated basis.

PART I

Item 1. Business.

We are a life sciences company dedicated to improving life through the application of our pioneering, proprietary ARCUS genome editing platform. We leverage ARCUS in the development of our product candidates, which are designed to treat human diseases and create healthy and sustainable food and agricultural solutions. We are actively developing product candidates in three innovative areas: allogeneic CAR T cell immunotherapy, *in vivo* gene correction, and food. We are currently conducting a Phase 1/2a clinical trial of PBCAR0191 in adult patients with relapsed or refractory, or R/R, non-Hodgkin lymphoma, or NHL, or R/R B-cell precursor acute lymphoblastic leukemia, or B-ALL. PBCAR0191 is our first gene-edited allogeneic chimeric antigen receptor, or CAR, T cell therapy candidate targeting CD19 and is being developed in collaboration with Les Laboratoires Servier, or Servier. We have received orphan drug designation for PBCAR0191 from the U.S. Food and Drug Administration, or FDA, for the treatment of acute lymphoblastic leukemia, or ALL. Made from donor-derived T cells modified using our ARCUS genome editing technology, PBCAR0191 recognizes the well characterized tumor cell surface protein CD19, an important and validated target in several B-cell cancers, and is designed to avoid graft-versus-host disease, or GvHD, a significant complication associated with donor-derived, cell-based therapies. We believe that this trial, which is designed to assess the safety and tolerability of PBCAR0191 at increasing dose levels, as well as to evaluate anti-tumor activity, is the first U.S.-based clinical trial to evaluate an allogeneic CAR T therapy for R/R NHL. Furthermore, we believe that our proprietary, one-step engineering process for producing allogeneic CAR T cells with a potentially optimized cell phenotype, at large scale in a cost-effective manner, will enable us to overcome the fundamental clinical and manufacturing challenges that have limited the CAR T field to date.

In December 2019, we announced initial data from the ongoing Phase 1/2a clinical trial of PBCAR0191 in adult patients with R/R NHL and R/R B-ALL. A total of nine adult patients were reported in these initial Phase 1 trial results, including six with NHL (three treated at Dose Level 1 ($3x10^5$ cells/kg), or DL1, and three treated at Dose Level 2 ($1x10^6$ cells/kg), or DL2), and three with B-ALL (all treated at DL2). These data indicated no serious adverse events or dose limiting toxicities. In the NHL cohort, four of six patients demonstrated an objective tumor response by Lugano criteria at day 28, for an overall objective response rate of 67%, including three partial responses and one complete response. In the ALL cohort, one of three patients achieved a complete response at day 28 following treatment with PBCAR0191. As of December 31, 2019, dosing of patients at Dose Level 3 ($3x10^6$ cells/kg) was underway. Based on the data observed at DL1 and DL2, we filed a protocol amendment for this trial with the FDA in December 2019. The amended trial design is intended to specifically address key clinical questions. These include assessing the impact of higher total doses of cells on clinical activity and/or the impact of modified lymphodepletion on the ability to achieve durable clinical benefit with associated CAR T cell expansion and persistence. Following feedback from the FDA in late January 2020, the protocol amendment is now being implemented.

In September 2019, the FDA accepted our investigational new drug, or IND, application for our second allogeneic CAR T cell therapy product candidate, PBCAR20A, for which we expect to commence a Phase 1/2a clinical trial in the first quarter of 2020. PBCAR20A is wholly owned by us and targets the validated tumor cell surface target CD20. It will be investigated in subjects with NHL, chronic lymphocytic leukemia, or CLL, and small lymphocytic lymphoma, or SLL. A subset of the NHL patients will have the diagnosis of mantle cell lymphoma, or MCL, and we have received orphan drug designation for PBCAR20A from the FDA for the treatment of this disease. Based on the adverse events observed to date with PBCAR0191, the FDA has agreed to allow us to commence dosing with PBCAR20A directly at Dose Level 2, which we expect to accelerate the timing for our expected completion of the trial.

In January 2020, the FDA accepted our IND application for our third allogeneic CAR T cell therapy product candidate, PBCAR269A, for which we expect to commence a Phase 1/2a clinical trial in 2020. PBCAR269A is wholly owned by us and is designed to target the validated tumor cell surface target BCMA. It will be investigated in subjects with R/R multiple myeloma and we have received orphan drug designation from the FDA for this indication.

Also in January 2020, we announced that we expect to advance a program targeting the rare genetic disease primary hyperoxaluria type 1, or PH1 as our lead wholly owned *in vivo* gene correction program. PH1 affects approximately 1-3 people per million in the United States and is caused by loss of function mutations in the AGXT gene, leading to the accumulation of calcium oxalate crystals in the kidneys. Patients suffer from painful kidney stones which may ultimately lead to renal failure. Using ARCUS, we are developing a potential therapeutic approach to the treatment of PH1 that involves knocking out a gene called hydroxyacid oxidase 1, or HAO1, which acts upstream of AGXT. Suppressing HAO1 has been shown in preclinical models by us to prevent the formation of calcium oxalate. We, therefore, believe that a one-time administration of an ARCUS nuclease targeting HAO1 may be a viable strategy for a durable treatment of PH1 patients. In preclinical studies we have demonstrated in a mouse model of PH1 that administration of an ARCUS nuclease targeting HAO1 resulted in approximately 70% reduction in urine calcium oxalate levels. We have also demonstrated that ARCUS efficiently knocked out the HAO1 gene in non-human primates. We plan to select a clinical candidate for this program during 2020.

During the fiscal year ended December 31, 2019, we opened our Manufacturing Center for Advanced Therapeutics, or MCAT, which we believe is the first in-house current good manufacturing practice, or cGMP, compliant manufacturing facility dedicated to genome-edited, off-the-shelf CAR T cell therapy product candidates in the United States. MCAT will enable in-house production of three different drug substances: allogeneic CAR T cells, messenger RNA (including formulations development) and adeno-associated viral vectors. We are currently using this new manufacturing center to create clinical trial material to be used in our BCMA targeting allogeneic CAR T clinical trials beginning in 2020. We believe MCAT confers a number of strategic advantages including cost benefits, control of our manufacturing process, and strategic flexibility as we execute our clinical trials. In the longer term, we believe MCAT has the potential to be a commercial launch facility with the capacity to generate up to 10,000 doses of CAR T cell therapies and 4,000 doses of gene therapies per year.

Our Pipeline

Allogeneic CAR T Immunotherapy

We believe that we have developed a transformative allogeneic CAR T immunotherapy platform with the potential to overcome certain limitations of autologous CAR T cell therapies and significantly increase patient access to these cutting-edge treatments. Cancer immunotherapy is a type of cancer treatment that uses the body's immune system to fight the disease. CAR T is a form of immunotherapy in which a specific type of immune cell, called a "T cell", is genetically engineered to recognize and kill cancer cells. Current commercially available CAR T therapies are autologous, meaning the T cells used as the starting material for this engineering process are derived directly from the patient. As a consequence, the therapy is highly personalized, difficult to scale, and expensive. Our allogeneic approach uses donor-derived T cells that are gene edited using ARCUS and are designed for safe delivery to an unrelated patient. We believe that this donor-derived approach will allow us to consistently produce a potent product by selecting donors with high quality T cells and will lessen the product-to-product variability seen in autologous therapies. We are able to produce allogeneic CAR T cells at a large scale in a cost-effective manner and have the potential to overcome the "one patient: one product" burden of autologous CAR T cell therapies.

Leveraging the unique gene editing capabilities of ARCUS, we have developed a one-step cell engineering process for allogeneic CAR T cells that is designed to maintain naïve and central memory T cell phenotypes throughout the CAR T manufacturing process, which we believe to be important for an optimized CAR T therapy. Due to our one-step editing method and the decision early in the development of our allogeneic CAR T immunotherapy platform to invest in process development, we have scaled our manufacturing process and are currently producing allogeneic CAR T cells at large scale in accordance with good manufacturing practice, or GMP.

In February 2016, we entered into a development and commercial license agreement, as subsequently amended, with predecessor entities of Les Laboratoires Servier, or Servier, which we refer to as the Servier Agreement. Pursuant to this agreement we have agreed to perform early-stage research and development on individual T cell modifications for up to six unique antigen targets, the first of which was selected at the inception of the agreement. Upon selection of an antigen target, we have agreed to develop the resulting therapeutic product candidates through Phase 1 clinical trials and prepare the clinical supply of such product candidates for use in Phase 2 clinical trials. We have the ability to opt-in to a 50/50 co-development and co-promotion agreement in the United States on all licensed products under the Servier Agreement.

Our most advanced program, PBCAR0191, is an allogeneic CAR T cell therapy candidate targeting the well-validated tumor target CD19 and is being developed for the treatment of adult patients with NHL and B-ALL. CD19 is a protein that is expressed on the surface of B cells. The FDA has granted PBCAR0191 orphan drug designation for the treatment of ALL. In December 2019, we reported initial data from our ongoing Phase 1/2a clinical trial of PBCAR0191. A total of nine adult patients were reported in these initial Phase 1 trial results, including six with NHL (three treated at Dose Level 1 ($3x10^5$ cells/kg), or DL1, and three treated at Dose Level 2 ($1x10^6$ cells/kg), or DL2), and three with B-ALL (all treated at DL2). These data indicated no serious adverse events or dose limiting toxicities. In the NHL cohort, four of six patients demonstrated an objective tumor response by Lugano criteria at day 28, for an overall objective response rate of 67%, including three partial responses and one complete response. In the ALL cohort, one of three patients achieved a complete response at day 28 following treatment with PBCAR0191. As of December 31, 2019, dosing of patients at Dose Level 3 ($3x10^6$ cells/kg) was underway. Based on the data observed at DL1 and DL2, we filed a protocol amendment for this trial with the FDA in December 2019. The amended trial design is intended to specifically address key clinical questions. These include assessing the impact of higher total doses of cells on clinical activity and/or the impact of modified lymphodepletion on the ability to achieve durable clinical benefit with associated CAR T cell expansion and persistence. Following feedback from FDA in late January 2020, the protocol amendment is now being implemented.

***In vivo* Gene Correction.** Our goal is to cure genetic diseases by correcting the DNA errors responsible for causing them. *In vivo* gene corrections are gene corrections that take place in a living organism. We have advanced a deep portfolio of diverse programs toward *in vivo* efficacy and toxicity studies. We have generated a significant large animal dataset that we believe to be the most comprehensive of any in the field and have observed high-efficiency *in vivo* genome editing in non-human primates in our preclinical studies, as highlighted in our July 2018 publication in *Nature Biotechnology*. We believe this is the first peer-reviewed publication of *in vivo* genome editing data in non-human primates. In our preclinical studies, we observed the high-efficiency editing of the PCSK9 gene in non-human primates using ARCUS and, even at the highest dose, the treatment was observed to be well-tolerated. We have

continued to observe the subjects for over three years since initial dosing and the benefit of the treatment in these studies appears to be permanent, which we believe is due to modifications to the DNA itself.

In January 2020 we announced that we expect to advance a program for the treatment of the rare genetic disease PH1 as our lead wholly owned gene correction program, based on preclinical data we have generated demonstrating high efficiency knock out of the HAO1 target gene in non-human primates using ARCUS, and evidence from a mouse model of clinically meaningful biomarker changes using our approach. We expect to nominate a clinical development candidate for this program during 2020. In addition, we are party to a collaboration agreement with Gilead Sciences, Inc. ("Gilead") to co-develop an ARCUS-based product candidate that is designed to cure chronic hepatitis B infection. Submission of an IND to the FDA for this product candidate is currently targeted for 2021. We are also in the discovery stage for other *in vivo* indications: familial amyloid polyneuropathy, hemophilia A, autosomal dominant retinitis pigmentosa, lipoprotein lipase deficiency and familial hypercholesterolemia.

Food. Our food platform, which we operate through our wholly owned subsidiary, Elo Life Systems, or Elo, is an integrated suite of gene discovery and crop engineering technologies that is designed to generate products in collaboration with leading food producers. We have a team with in-depth experience in crop genome editing. Over the last decade, we have worked with some of the largest plant biotechnology companies to edit gene targets and develop potential product candidates in a variety of crop plants. By combining the power of our ARCUS technology platform with target discovery, transformation and high throughput trait evaluation, we are enabling our partners to potentially address critical issues in food and agriculture created by climate change and dramatic shifts in consumer preference toward healthier eating. Our collaboration-driven business model enables us to remain capital efficient throughout the product development cycle while generating revenue through various revenue-sharing models. For example, since 2014, Elo and Cargill have been engaged in a collaboration to produce ARCUS-optimized canola varieties and have achieved significantly lower levels (less than 4.5%) of saturated fatty acids compared to the current levels (7%) in greenhouse studies. Elo achieved proof of concept with its ZeroMelon™ watermelon-based sweetener program. This program is intended to leverage ARCUS to develop a scalable low-calorie sweetener. Elo will continue to advance the ZeroMelon program towards greenhouse trials in 2020. Prior to commercialization of any of our food product candidates, we must complete greenhouse studies and multiple phases of field testing.

Our Team

We believe that our team, whom we call Precisioneers, has among the deepest scientific experience and capabilities of all genome editing companies. Derek Jantz, Ph.D., our Chief Scientific Officer and a co-founder of Precision, and Jeff Smith, Ph.D., our Chief Technology Officer and also a co-founder of Precision, have been working with genome editing technology for more than 15 years. They are pioneers in the genome editing field and developed our ARCUS genome editing platform to address what they perceived as limitations in the existing genome editing technologies. Our Chief Executive Officer, Matthew Kane, also a co-founder of Precision, has almost 20 years' experience in life sciences, most of which has been working in genome editing.

We have selectively expanded our team of Precisioneers to include individuals with extensive industry experience and expertise in the discovery, development, manufacture and commercialization of cell and gene therapies and the creation of innovative solutions to myriad problems affecting food systems. Our team of Precisioneers includes more than 62 scientists with Ph.D. degrees.

We are a purpose-driven organization, and we have carefully promoted a culture that values innovation, accountability, respect, adaptability and perseverance. We strive to ensure that our open, collaborative culture empowers Precisioneers to be their best selves and do their best work. We strongly believe that our shared values will help our team navigate and overcome any challenges we may experience as we pursue our mission of improving life through genome editing. Our culture has helped build a world-class team with industry-leading experience in genome editing and continually attracts new talent to further build our capabilities. Our team is a group of motivated individuals that value the opportunity to contribute their time and talents toward the pursuit of improving life. Precisioneers appreciate high-quality research and are moved by the opportunity to translate their work into treatments and solutions that will impact human health.

Our Strategy

We are dedicated to improving life. Our goal is to broadly translate the potential of genome editing into permanent genetic solutions for significant unmet needs. Our strategy to achieve this goal includes the following key elements:

- **Create a fully integrated genome editing company capable of delivering solutions that address unmet needs impacting human health.** We believe that, to be a leader in the field of genome editing and maximize the impact of our ARCUS genome editing platform, we must be able to control those elements of our business that may provide us with certain strategic advantages or operational efficiencies. We intend to continue to invest in comprehensive research, development, manufacturing and commercial capabilities that provide control and oversight of our product candidates from discovery through commercialization.

- **Capitalize on our emerging leadership position in allogeneic CAR T immunotherapies.** We believe that we have developed the first allogeneic CAR T cell platform capable of producing drug product at scale, with a potentially optimal cell profile for therapeutic efficacy and true off-the-shelf delivery without the need for harsh and potentially toxic lymphodepletion. We have selected three validated CAR T cell targets that we believe offer the greatest chance of clinical success for our initial product candidates, which we aim to rapidly advance through and into clinical development. In December 2019, we reported initial data from the first six patients with advanced NHL and first three patients with advanced ALL treated with PBCAR0191 at the lowest two dose levels in our ongoing Phase 1/2a clinical trial. These initial data indicated no serious adverse events or dose-limiting toxicities, and demonstrated initial evidence of cell-mediated anti-tumor activity. As of December 31, 2019, dosing of patients at the third dose level was underway. Our CAR T platform is modular, which we believe will allow us to leverage proof-of-concept from our ongoing and planned initial human trials for multiple other CAR T programs. We believe the combination of these factors, along with our unique ARCUS technology, puts us in a differentiated position to be the leader in the development of allogeneic CAR T therapies.

- **Advance ARCUS-based *in vivo* gene correction programs into human clinical trials.** In our preclinical studies, we observed the high-efficiency and tolerability of *in vivo* genome editing using ARCUS in a non-human primate model, as published in *Nature Biotechnology* in July 2018. To our knowledge, we are the first company to complete this milestone, which we believe to be critical to successful *in vivo* genome editing therapeutic development. We have built on this early success by diligently advancing a diverse portfolio of preclinical *in vivo* gene correction programs through additional large animal studies, focusing initially on gene targets occurring in the liver and eye. Based on the results from these studies, we are advancing our lead wholly owned *in vivo* gene correction program for the rare genetic disease primary hyperoxaluria type 1.

- **Build a food business focused on developing products designed to improve human health and respond to the impacts of climate change.** We believe that rapidly changing consumer preferences and food insecurity resulting from population growth and climate change will drive significant demand for genome-edited food products. We are building a fully integrated discovery and development platform that combines genome editing, gene discovery, plant transformation and high-throughput testing to enable accelerated innovation in the food industry. We employ a business model that is focused on collaborating with critical stakeholders within the supply chain from the outset of any given project. We believe that this approach will enable us to successfully respond to growing unmet needs within food supply to build a human health-focused business in a capital-efficient manner.

- **Continue investing in the optimization of ARCUS and enabling technologies.** We believe that a key to our future success is the quality of the genome editing tools that we produce. Since our founding, we have devoted ourselves to continuously refining the precision and efficiency of our core genome editing platform. We intend to continue this investment in ARCUS while surrounding it with enabling technologies and expertise to retain what we believe is a leadership position in the field.

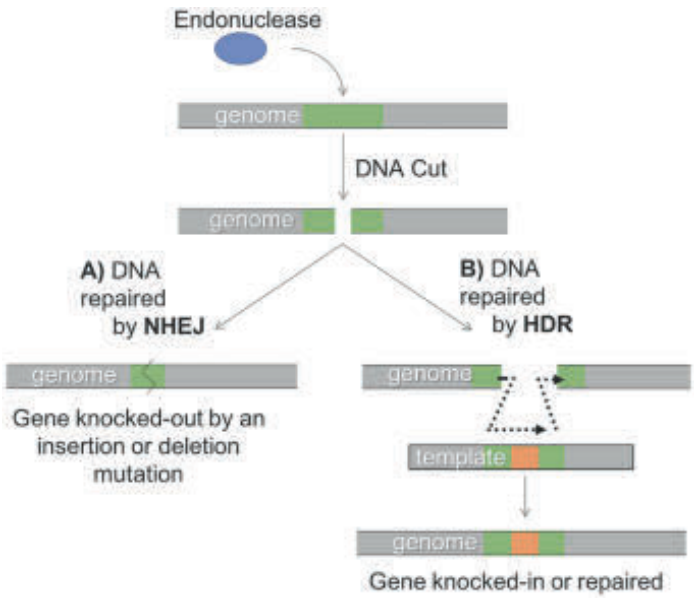
- **Create an environment that is a destination of choice for premier talent within the life sciences industry.** We believe that we currently have among the deepest and strongest skill set within the genome editing industry and credit much of our past success to our commitment to our team and culture. Our future success will depend on our ability to continue to attract and retain world-class talent within our markets of interest. We intend to consciously invest in fostering an environment within our company that is both challenging and supportive and inspires our team to broadly translate genome editing into permanent genetic solutions.

- **Expand the breadth of our operations through additional product platforms and strategic relationships.** We believe that the ARCUS genome editing platform has broad utility beyond our current areas of focus. We intend to invest in the development of additional product platforms and seek collaborations with companies with additive expertise in areas outside of our current target markets to maximize the value of our company.

Overview of Genome Editing

Deoxyribonucleic acid, or DNA, carries the genetic instructions for all basic functions of a living cell. These instructions are encoded in four different molecules, called bases, which are strung together in specific sequences to form genes. Each gene is responsible for a specific function in a cell, and the complete set of genes in a cell, which can consist of tens of thousands of genes and billions of individual bases, is known as a genome. The complete genome sequence has been determined for many organisms, including humans. This allows scientists to identify specific genes and determine how their unique sequences contribute to a particular cellular function. Studying variations in gene sequences further informs an understanding of why a cell behaves a certain way, which can greatly enhance understanding of what causes and how to treat aberrant behavior that leads to disease.

Genome editing is a biotechnology process that removes, inserts or repairs a portion of DNA at a specific location in a cell's genome. Early applications of genome editing focused on advancing genetic research. As genome editing technologies have advanced, their application is moving beyond understanding disease to treating or preventing disease by editing DNA. Genome editing is accomplished by delivering a DNA cutting enzyme, called an endonuclease, to a targeted segment of genetic code. Once the endonuclease cuts the DNA, the cell has to repair the break to survive and will generally do so in one of two ways, as shown below.



There are two primary mechanisms of DNA repair, non-homologous end joining, or NHEJ, and homology directed repair, or HDR. As shown in A) above, NHEJ is a pathway that repairs breaks in DNA without a template. NHEJ is the less precise method of repair that prioritizes speed over accuracy, making it prone to leaving insertions and/or deletions of DNA bases at the cut site. These insertions or deletions can disrupt the gene sequence and can be used to inactivate or "knock out" the function of the gene. Accordingly, genome editing technologies can be used to permanently knock out a gene in a cell or organism by creating a break in the DNA sequence of that gene.

As shown in B) above, HDR is a mechanism of DNA repair whereby the cell uses a second DNA molecule with a sequence similar to that of the cut DNA molecule to guide the repair process. Since HDR uses a "template" of similar genetic information to guide the repair process, it is the more precise mechanism of cellular repair. HDR results in the sequence of the template being copied permanently into the genome at the site of the DNA cut. If we provide a template DNA molecule directly to the edited cell and the cell repairs itself using HDR, a new gene can be incorporated or "knocked in" at a precise location in the genome. Alternatively, the use of HDR can "repair" a DNA mutation by correcting it to the proper functioning sequence when repairing the break. Thus, genome editing endonucleases can be used to introduce a variety of different changes to the genetic code of a cell or organism including gene knockout, gene insertion and gene repair.

There are several genome editing technologies, including ARCUS, zinc-finger nucleases, or ZFNs, TAL-effector nucleases, or TALENs, and CRISPR/Cas9. These technologies differ from one another principally in the properties of the endonuclease that they each employ. The different endonucleases have fundamentally different mechanisms of recognizing and cutting their DNA targets, which gives each technology advantages and disadvantages depending on how each is used.

Our Approach to Genome Editing

We are pioneers in the field of genome editing and have extensive experience with a breadth of genome editing technologies. Our ARCUS platform was developed to address limitations of other editing technologies that could impair their deployment for therapeutic applications. We looked to nature for examples of genome editing and found the I-CreI endonuclease from the algae *Chlamydomonas reinhardtii*. Unlike ZFN, TALEN or CRISPR/Cas9, I-CreI is a natural enzyme that evolved to edit a large, complex genome. In nature, it is responsible for modifying a specific location in the algae genome by inserting a gene using the HDR process, according to scientific literature.

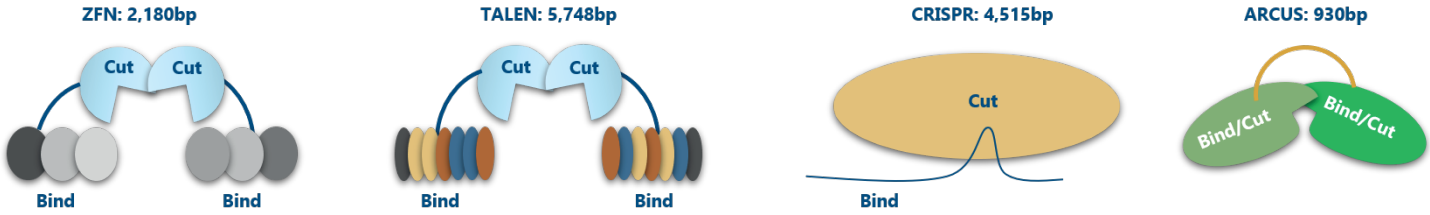
We believe that I-CreI has a number of attributes that make it attractive for the development of novel genome editing endonucleases, such as:

- **Specificity.** Complex genome editing applications, especially those involving the human body, require a high level of endonuclease specificity to limit the likelihood that the endonuclease will recognize and edit any genetic sequence other than its intended target. Based on scientific literature, we believe that several attributes of I-CreI naturally inhibit off-target cutting. I-CreI:

Recognizes and cuts a DNA sequence in the genome of algae that is 22 base pairs in length. A sequence of this length is statistically expected to occur only once in a large genome.

Recognizes its DNA target site through a large number of complex molecular interactions with the bases. Relative to other endonucleases, an unusually high percentage of the I-CreI protein surface area is dedicated to specific contacts with the DNA bases. This method of site recognition enhances I-CreI's ability to discriminate among similar sequences of DNA, reducing the likelihood that it will cut DNA sequences that differ even slightly from the intended DNA sequence.

Physically couples the functions of DNA binding and DNA cutting. The region of I-CreI that is responsible for DNA site recognition also contains the region that cuts the DNA, or the active site. Due to this structure, the active site is not in a position to cut unless the enzyme is seated properly on the correct DNA sequence. ZFN, TALEN and CRISPR/Cas9 are multi-domain endonucleases in which the DNA-binding and DNA-cutting functions reside in different regions of the enzyme.



Remains inactive in the absence of its DNA target site. When I-CreI is not bound to its proper DNA target site, it folds up on itself such that its active site is blocked from external interaction. In this form, I-CreI is inert. This structural configuration provides a type of natural "on/off switch" that reduces I-CreI's activity away from the target site. Other genome editing endonucleases lack this type of natural control over the enzyme's cutting activity.

Cuts slowly and with low turnover. Relative to other genome editing endonucleases and to enzymes in general, I-CreI has a very slow mechanism of action. I-CreI takes a relatively long time to cut its DNA target site and, after doing so, remains bound to the cut DNA ends. These properties greatly reduce the likelihood that I-CreI will cut any other DNA site after making its initial on-target cut. We believe that this translates directly to a reduction in the frequency of off-target cutting without sacrificing on-target editing efficiency. In contrast, other editing endonucleases have high rates of catalysis and turnover because their natural function is defending bacteria from viruses.

- **Efficiency.** Most applications of genome editing technology require that a sufficient portion of the targeted cells are edited to achieve the desired result. The activity level of the endonuclease is one factor that can affect how many cells are edited. The slow catalytic mechanism of I-CreI imparts specificity but does not impact its on-target efficiency for genome editing purposes because genome editing involves cutting only a single site in a cell. As such, I-CreI is able to achieve a high level of on-target editing while rarely cutting off-target, as supported by scientific literature.

- **Delivery.** Size and structural simplicity affect the ease with which endonucleases can be delivered to cells for editing. I-CreI is very small relative to other genome editing endonucleases. It is approximately one quarter to one sixth of the size of the ZFN, TALEN and CRISPR/Cas9 endonucleases. Unlike those endonucleases, I-CreI can be delivered as a single gene. As such, we believe it is compatible with many different delivery mechanisms. Additionally, I-CreI's size and structure facilitate

the simultaneous delivery of multiple engineered endonucleases to introduce more than one edit to a cell. Both of these properties significantly broaden the spectrum of potential applications for I-CreI-based genome editing endonucleases.

- **Type of Cut.** The three prime, or 3', overhangs created when I-CreI cuts DNA have been shown to promote DNA repair through a mechanism called "homology directed repair," or HDR. 3' overhangs are stretches of unpaired nucleotides in the end of a DNA molecule. A genome editing technology that facilitates cellular repair through HDR enables applications that require a gene insertion or gene repair. Unlike other editing endonucleases, I-CreI creates four base 3' overhangs when it cuts its DNA site, which increases the likelihood that the cell will repair the DNA cut through HDR. As such, the DNA cuts created by I-CreI can be exploited to efficiently insert or repair DNA, consistent with the natural role of I-CreI in catalyzing the targeted insertion of a gene in algae.

- **Programmability.** I-CreI recognizes its DNA target site through a complex network of interactions that is challenging to re-program for new editing applications involving different DNA sequences. The challenges associated with re-programming I-CreI have, historically, hampered its adoption by the genome editing community in favor of more easily engineered endonucleases. This engineering challenge represents a high barrier to entry and has enabled us to secure a strong intellectual property position and control over what we believe to be a superior genome editing technology.

Other than the key programming challenge, we believed that the differentiated properties of I-CreI cited above made it an ideal "scaffold" for the development of novel genome editing tools. Moreover, we believed those properties were differentiated enough from other editing technologies to merit substantial investment in overcoming the key challenge of programmability. To that end, we invested 15 years of research effort to develop a robust, proprietary protein engineering method that now enables us to consistently re-program I-CreI to direct it to targeted sites in a genome. We call our approach ARCUS.

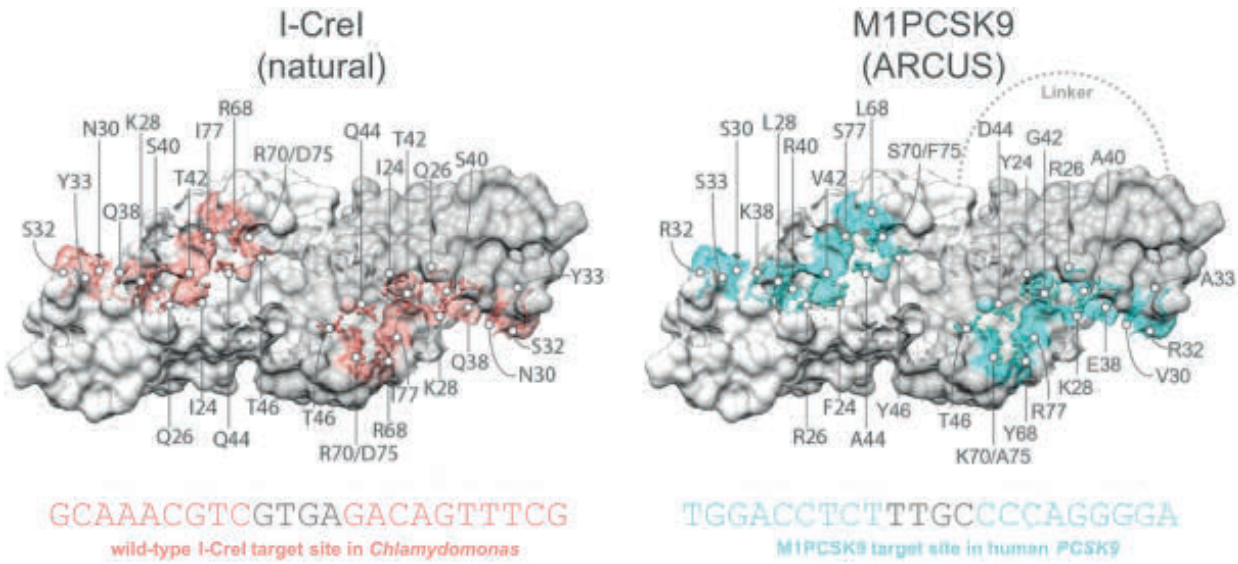
Our ARCUS Genome Editing Platform

ARCUS is a collection of protein engineering methods that we developed specifically to re-program the DNA recognition properties of I-CreI. In nature, the I-CreI endonuclease recognizes and cuts a DNA sequence in the genome of algae. To apply I-CreI to genome editing in other cells or organisms, we must modify it to recognize and cut a different DNA sequence for each new application we pursue. Since the I-CreI endonuclease evolved to recognize its target sequence in the algae genome with a high degree of selectivity, as supported by scientific literature, it was necessary for us to develop sophisticated protein engineering methods to re-engineer I-CreI endonucleases to bind and cut a different DNA sequence. Using the ARCUS process, we create customized endonucleases for particular applications. We call these custom endonucleases "ARCUS nucleases." Our process is proprietary and core components are claimed in an extensive international patent portfolio. Moreover, since the ARCUS process involves a sophisticated blend of protein engineering art and science, each ARCUS nuclease we create is novel and, we believe, patentable. As of December 31, 2019, we have obtained U.S. patents with claims directed to three ARCUS nucleases as compositions of matter, and currently claim over 270 ARCUS nucleases as compositions of matter in pending U.S. and foreign patent applications.

Our objective with ARCUS is to redirect I-CreI to a new location in a genome without compromising its editing abilities. To accomplish this, we modify the parts of the enzyme that, as reported by scientific literature, are involved in recognizing the specific DNA target site. These enzyme parts are also reported to comprise the I-CreI active site and to be involved in anchoring the enzyme to its DNA site in the algae genome. In our preclinical studies, we have observed that these modifications allowed us to control how tightly an engineered variant of I-CreI binds to its intended DNA site, as well as how quickly it cuts, in a plant or animal cell. By adjusting these two parameters, we observed that we can generally control the efficiency with which the engineered endonuclease cuts its intended target site or any potential off-target sites.

The natural I-CreI target site is pseudo-palindromic, meaning the first half of the sequence is approximately a mirror image of the second half of the sequence. Palindromic DNA sites are rare in most genomes so it was necessary for us to develop additional technology that would overcome this limitation on the diversity of DNA sites that we can target. To this end, the ARCUS process involves the production of *two* re-programmed I-CreI proteins for each target site. These two different proteins are then linked together into a single protein that can be expressed from a single gene. This approach, called a "single-chain endonuclease," represents a major advancement in I-CreI engineering because it enables our ARCUS nucleases to recognize and cut *non*-palindromic target sites using an endonuclease that, like natural I-CreI, is very small and easy to deliver to cells.

The graphic below depicts the molecular structure of natural I-CreI in comparison to an engineered ARCUS nuclease called "M1PCSK9." The regions of the structures colored in pink or cyan represent the amino acid building blocks that are responsible for contacting the DNA target site and determining the sequence of DNA bases that the endonuclease recognizes and cuts. The DNA target sites recognized by the two endonucleases are shown below the structures.

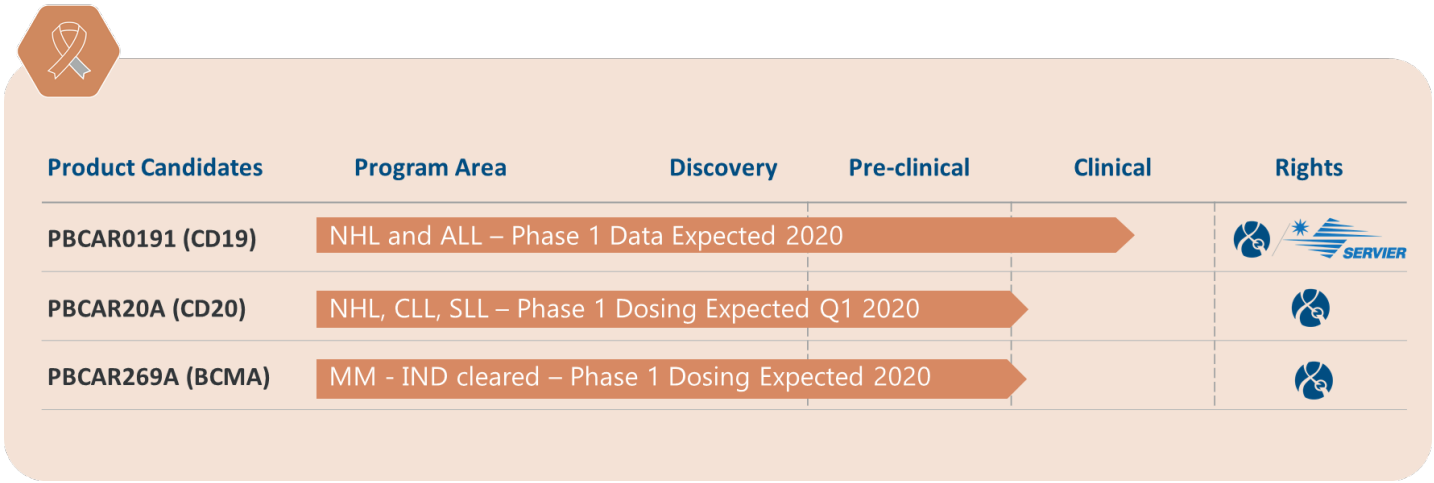


Since creating an ARCUS nuclease requires such extensive reengineering of I-CreI, it is, generally, an iterative process that involves multiple cycles of design and testing. We can typically produce a first-generation ARCUS nuclease in seven weeks. First-generation nucleases are suitable for research and development, proof-of-concept studies or other non-therapeutic applications. For therapeutic applications requiring the lowest possible off-targeting, however, we are rarely satisfied with generation one and each endonuclease undergoes extensive optimization. To this end, we thoroughly interrogate the nuclease with respect to its on-and off-target cutting properties using ultra-sensitive tests that we developed specifically for use with ARCUS. These results then inform our design of a second-generation nuclease with the goal of optimizing on-target efficiency while minimizing off-target cutting. Therapeutic ARCUS nucleases typically require two to four cycles of design and testing, often resulting in off-target cutting frequencies that are below the limit of detection with our most sensitive assays. This process can take six months or longer and has resulted in development of "therapeutic-grade" editing endonucleases.

The ARCUS process is robust and reproducible. It enables us to create engineered variants of the I-CreI endonuclease that recognize and cut DNA sites that bear little resemblance to I-CreI's natural target site. Importantly, however, ARCUS retains the attributes of I-CreI that we believe make it highly suitable as a genome editing endonuclease for complex commercial applications. We expect ARCUS nucleases to be exquisitely specific as a result of the natural structure of I-CreI and the intricate design process we employ to create them. We believe ARCUS nucleases are the smallest and easiest to deliver genome editing endonucleases. Like I-CreI, in our preclinical studies, ARCUS nucleases have been observed to produce DNA cuts with 3' overhangs that promote HDR, facilitating gene insertions and gene repairs in addition to gene knockouts. We believe that these attributes will enable us to translate ARCUS into patient-based clinical trials and a wide array of product candidates that have the potential to address the limitations of other genome editing technologies and improve life.

We believe that ARCUS is a leading genome editing platform for therapeutic and food applications. Realizing the potential of ARCUS, however, requires supporting technologies and capabilities. To facilitate the potential commercial deployment of ARCUS in different fields, we surround it with ancillary technologies, domain expertise and infrastructure specific to that area of development. Our goal is to leverage ARCUS to build additional product-development platforms designed to rapidly generate new products in a given field. We are currently developing products from three such platforms: allogeneic CAR T immunotherapy, *in vivo* gene correction, and food.

Our Allogeneic CAR T Immunotherapy Platform



We are leveraging the properties of ARCUS in an integrated platform for the development and large-scale production of off-the-shelf (allogeneic) CAR T cell immunotherapies. A key to the success of this platform is our proprietary, one-step method for modifying the genetics of T cells from a healthy donor to make them detect and kill cancer cells. This method allows us to produce allogeneic CAR T therapy candidates with a potentially optimal phenotype for clinical development and scaled manufacturing. We have demonstrated that our approach yields an allogeneic product with a high proportion of so-called naïve and central memory CAR T cells, which are the T cell phenotypes that have previously correlated best with good clinical benefit and fewer adverse events compared with terminally differentiated effector T cells. Additionally, because these cells are derived from healthy donors and maintain the phenotypic characteristics described, it is our hypothesis that they will be more capable of controlled *in vivo* expansion and tumor killing without requiring harsh lymphodepletion regimens to be administered to the patient. As such, we believe that our allogeneic CAR T cell platform will greatly increase patient access to these cutting-edge treatments.

CAR T Cell Therapies

CAR T cell therapy is a form of cancer immunotherapy that uses a patient's immune system to kill cancer cells. T cells are a component of the immune system that can distinguish pathogen-infected or tumor cells from healthy cells and kill them. Recognition of pathogen-infected cells or tumor cells occurs through a protein called a T cell receptor, or TCR, that is expressed on the surface of T cells. Tumor cells, however, have evolved numerous ways to evade TCR-mediated killing by T cells. In CAR T cell therapy, T cells are engineered *ex vivo* to express a protein called a chimeric antigen receptor, or CAR, that recognizes specific tumor cell surface targets and allows the T cells to function independently of the TCR, thus circumventing tumor cells' evasion of the TCR. CAR T cell therapy has been shown in clinical trials to be an effective treatment for patients who have not responded to traditional cancer treatments, and there are now two FDA approved CAR T cell products available to treat certain types of leukemia and lymphoma.

The most common form of CAR T cell therapy, which includes the two approved therapies, is referred to as "autologous" CAR T cell therapy because the CAR T cells are generated using T cells taken directly from the cancer patient. T cells are harvested from the patient, genetically engineered *ex vivo* to express a CAR, and then injected back into the patient. While autologous CAR T cell therapy has been shown to be effective for treating certain tumor types, it has several significant drawbacks:

- **Patient eligibility.** Many patients may not be eligible for the treatment because their cancer has lowered their T cell numbers and T cell quality, or because the risk of undergoing the process to harvest T cells is too great.

- **Consistency.** Since each autologous therapy is, by definition, unique, it is difficult to define standards of safety and efficacy or to thoroughly assess the quality of the product prior to infusion into the patient.

- **Delay in treatment.** Because the process to make autologous CAR T cells can take several weeks, there is a significant delay in treating what can often be very aggressive tumors. Patients' disease often progresses before they can receive the CAR T therapy, or if manufacturing complications such as contamination, mislabeling or low yield are encountered, the patient may not survive long enough to attempt manufacturing a second time.

- **Cost.** The autologous CAR T cell manufacturing process is complex and expensive and must be performed, in its entirety, for each patient. As such, scaling of the manufacturing process is exceedingly difficult, and the cost of product manufacturing has resulted in high treatment costs per patient. This high cost of treatment, along with the practical complexities described above, limits the availability of autologous CAR T cell therapies to patients.

We believe that the use of allogeneic, or donor-derived, CAR T cells will address many of the challenges associated with autologous CAR T cell therapy. An allogeneic approach allows selection of donors using specific criteria to define "healthy" T cells possessing specific phenotypes, which we believe are important to clinical efficacy and which may lessen the product-to-product variability seen in autologous therapies. Donor-derived cells could be used in any patient, eliminating the "one patient: one product" burden of autologous CAR T cell therapies. Because healthy donors would provide the starting material, patients that were too sick or otherwise unqualified for an autologous approach may benefit from an allogeneic CAR T cell therapy. Additionally, patients receiving an off-the-shelf allogeneic treatment would not have to wait for the manufacture of a personalized autologous treatment, which could be further delayed by manufacturing difficulties. By scaling the manufacturing of CAR T cells and optimizing the manufacturing process for a specific pool of donors, we believe that allogeneic CAR T cells can be manufactured at costs that are significantly lower than autologous CAR T cells and that will, over time, approach the manufacturing costs for conventional biologic drugs. These potential advantages of an allogeneic approach should allow for a safer, more predictable product with defined quality standards and significantly increase patient access.

The major challenge to producing allogeneic CAR T cells is that donor-derived T cells still express their own TCR. Because the TCR enables T cells to recognize cells that are foreign to the donor, they may induce GvHD if introduced to the patient in their natural form. This is a dangerous condition in which the donor T cells indiscriminately attack cells in the body of the patient. Accordingly, expression of the TCR must be eliminated in donor cells before the cells can be engineered into CAR T cells and administered to a patient. An allogeneic CAR T cell therapy therefore requires the use of a genome editing technology like ARCUS to knock out TCR genes in the T cell DNA to produce "universal" donor cells that are designed to be incapable of eliciting GvHD.

We and others have shown that genome editing can be used to eliminate expression of the TCR on donor cells, and there are several companies working on gene-edited allogeneic CAR T cell therapies. However, there are a number of challenges associated with manufacturing gene-edited allogeneic CAR T cells, including the following:

- **T cell phenotype.** T cells actually comprise several subtypes of different cells. Some subtypes of T cells are directly responsible for killing virus-infected or tumor cells, while other subtypes serve a helper function. Some subsets retain a "memory" function and can be recalled later if the target tumor reappears, and some subsets even decrease the killing activity of T cells. T cells undergo a process of differentiation in response to contact with their targets, which leads to young, naïve and central memory T cells changing into "terminally differentiated" or "effector" T cells. These effector T cells are good at killing pathogen-infected cells and other foreign cells, but do not survive for long periods of time in the body and are poorly expansile, in contrast to naïve and central memory T cells. T cell subsets are distinguished by the unique combination of proteins they express on their cell surface, which is described as their "phenotype." Understanding what phenotypes of T cells are best for a CAR T cell therapy is important, as is the ability to maintain the stability of those phenotypes throughout the manufacturing process. The more genetic and other manipulation T cells undergo, the more likely they are to differentiate from the naïve and central memory phenotype into terminally differentiated cells. This can happen over the course of a manufacturing run, with the length of the process being directly related to the final cell phenotype. As a result, the final CAR T product may not comprise the desired mix of T cell subtypes for clinical development.

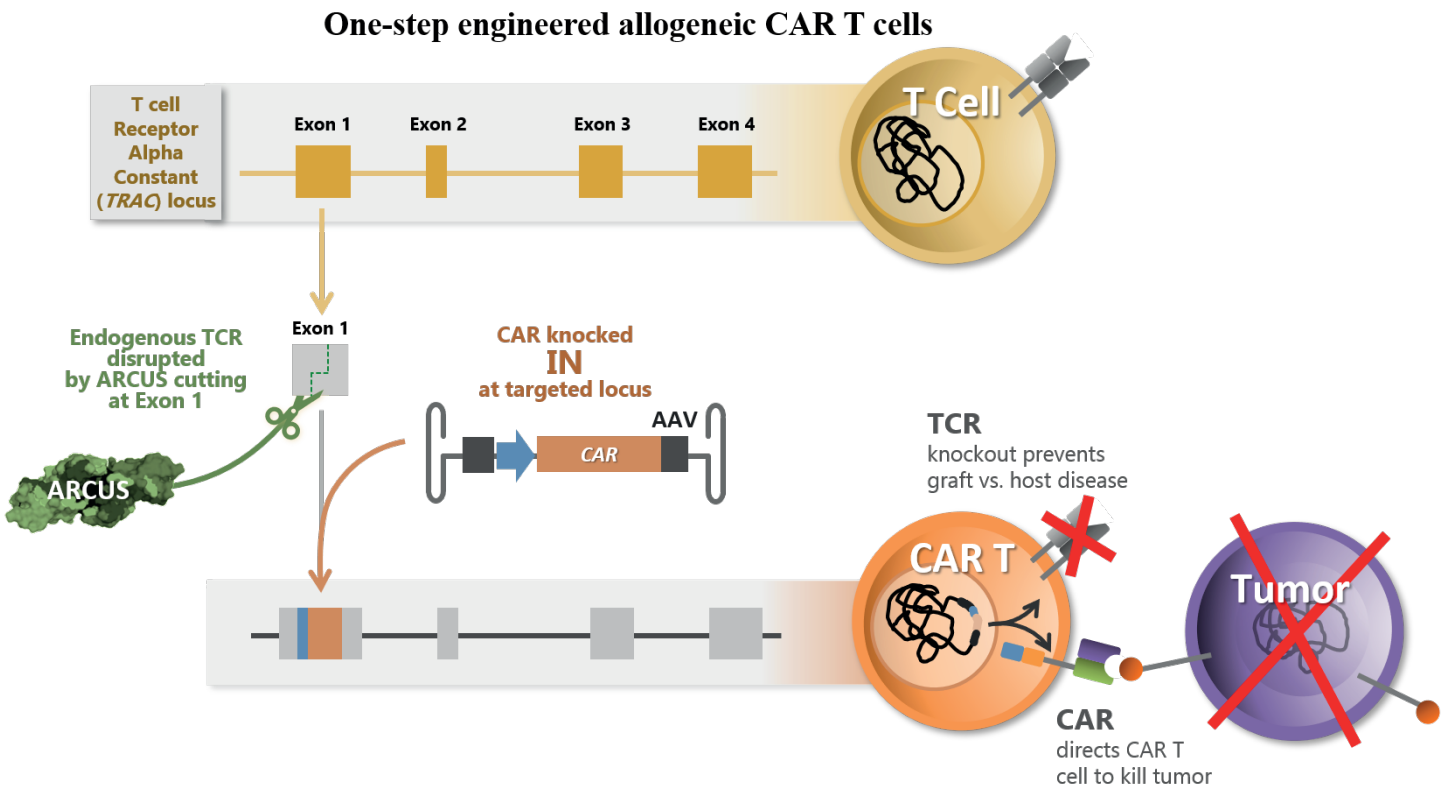
- **Consistency.** In most CAR T cell therapies, the CAR is introduced into the T cell using a viral vector, usually a lentiviral vector. Lentiviral vectors are retroviruses that are typically engineered to insert DNA, in this case the gene encoding a CAR, into a random location in the genome of a cell. When introduced in this manner, CAR expression typically varies significantly from cell-to-cell depending on the number of CARs that were delivered and where in the T cell genome they were inserted. This variability can cause CAR T cells to be inconsistent from cell-to-cell within the same CAR T cell batch. Too little expression could make the CAR T cell unable to activate and kill when it identifies a cancer cell. Too much expression could lead the CAR T cell to become hyper-stimulated, which can lead to an inactive state known as "exhaustion."

- **Scalability.** Manufacturing scale drives the cost and availability of the final off-the-shelf product. While generating allogeneic CAR T cells at lab scale (a few million cells) is relatively straightforward, manufacturing them at a clinically relevant scale (billions of cells) is a major challenge that is impacted by, among other things, the efficiency of CAR gene insertion, the efficiency of on- and off-target genome editing, starting donor T cell phenotype and the duration of the manufacturing process.

Our Approach to Allogeneic CAR T Cells

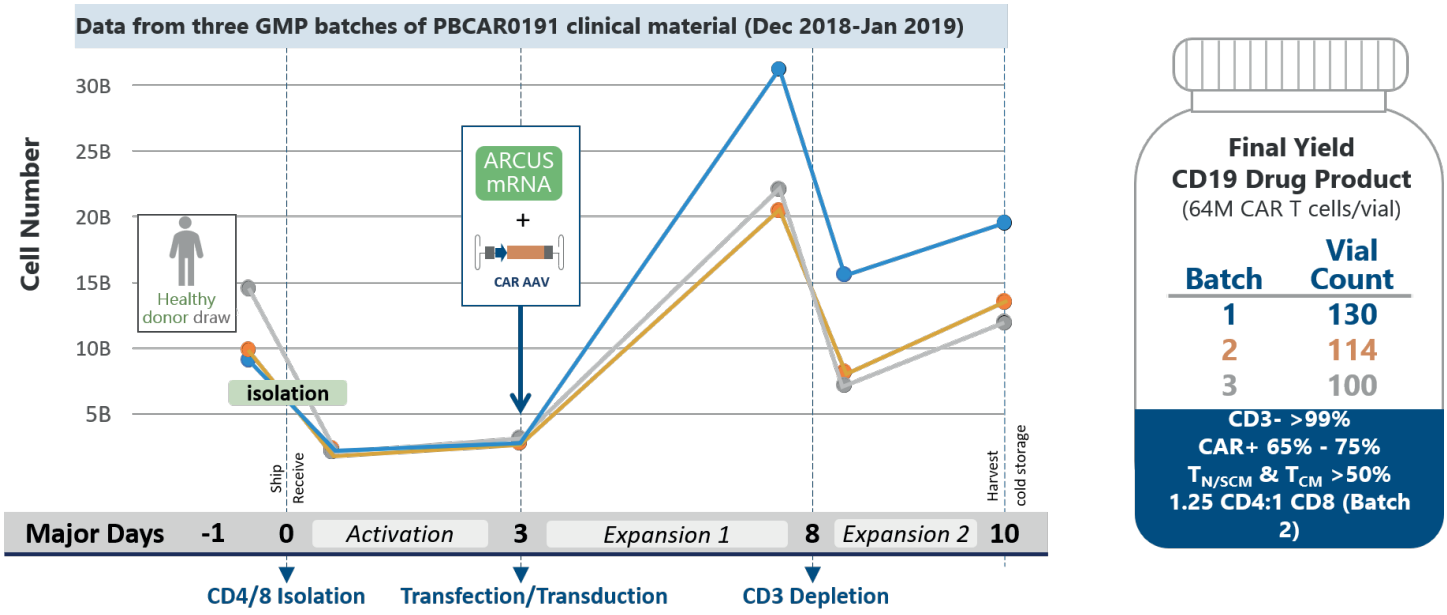
We have used the unique qualities of ARCUS to create a one-step cell engineering process for allogeneic CAR T cells that we believe yields a well-defined cell product and is designed to maintain naïve and central memory T cell phenotypes throughout the CAR T manufacturing process; we believe this is of paramount importance for an optimized CAR T therapy. To produce an allogeneic CAR T cell, it is necessary to make two changes to the DNA of T cells from a healthy donor. First, it is necessary to knock out the gene that encodes the TCR to prevent the donor-derived T cells from eliciting GvHD in the patient. The TCR is actually a complex of several

different components encoded by different genes, and knocking out any one of them is generally sufficient to prevent the TCR from functioning. Second, it is necessary to add, or knock in, a gene that encodes the CAR to give the T cells the ability to recognize and kill cancer cells. We developed a proprietary, one-step method for achieving both genetic changes simultaneously. This method, aspects of which are protected by nine issued U.S. patents, involves the use of ARCUS to target the insertion of a CAR gene directly into the gene that encodes the alpha subunit of the TCR. This approach adds the DNA encoding the CAR while simultaneously disrupting the DNA encoding the TCR, essentially replacing one gene with the other.

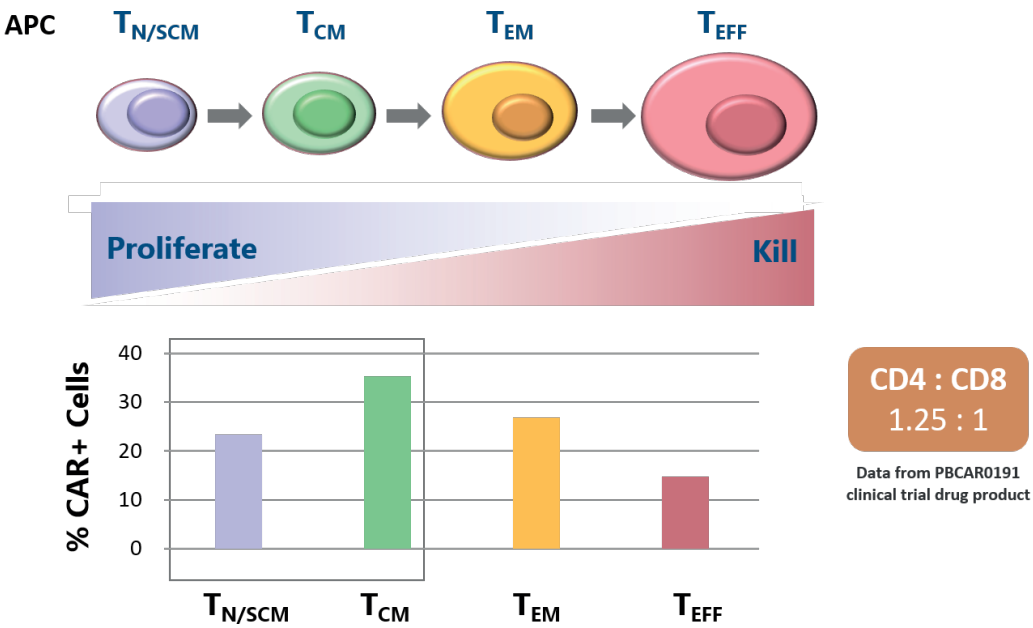


We believe that our one-step engineering approach, and the differentiated attributes of the ARCUS nuclease used to implement it, will overcome many of the critical challenges associated with allogeneic CAR T cell production as follows:

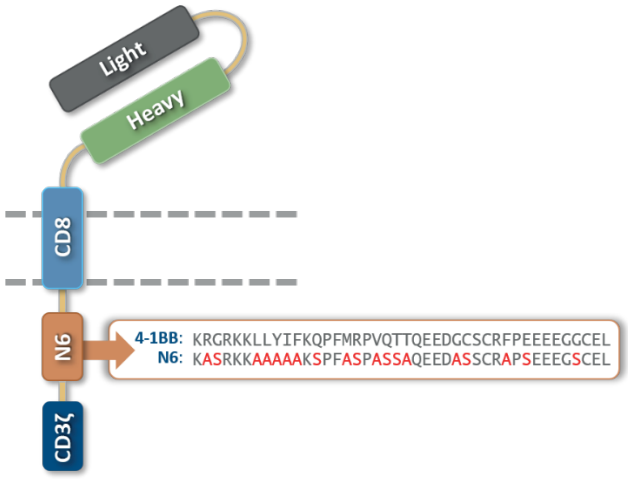
- **T cell phenotype.** According to scientific literature, T cell phenotype has a profound impact on the efficacy of CAR T cell therapy. Specifically, "young" CAR T cells with naïve and central memory phenotypes have been observed to undergo the most robust expansion following administration, which leads to a therapeutic effect. Therefore, we have established a T cell platform that is designed to maximize the percentage of cells with these ideal phenotypes. Our process starts with carefully screening donors to identify individuals with high percentages of naïve or central memory T cells and a ratio of CD4:CD8 T cells that we believe should yield the most potent cell product. To this end, we have developed our own set of analytics for screening candidate donors and have put significant effort into identifying individuals with the desired T cell profiles. We then use proprietary growth strategies and media to maintain naïve and central memory T cell phenotypes throughout the CAR T manufacturing process. We believe this is of paramount importance for an optimized CAR T therapy. Importantly, our one-step genome editing approach avoids making multiple breaks to the T cell's DNA and also contributes to minimizing cell processing time, which helps prevent the CAR T cells from differentiating during the process. We believe our 10-day allogeneic manufacturing process is the shortest in the industry. The figure below shows results from three full-scale manufacturing campaigns, each of which produced a GMP batch of PBCAR0191.

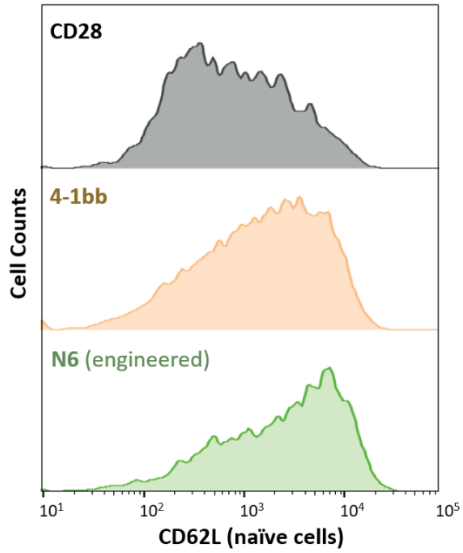


The figure below shows phenotype data from PBCAR0191 CAR T cells that were produced as drug product for our ongoing Phase 1/2a clinical trial in adult patients with R/R NHL and R/R B-ALL. The drug product comprises mostly naïve ($T_{N/SCM}$) and central memory (T_{CM}) T cells.

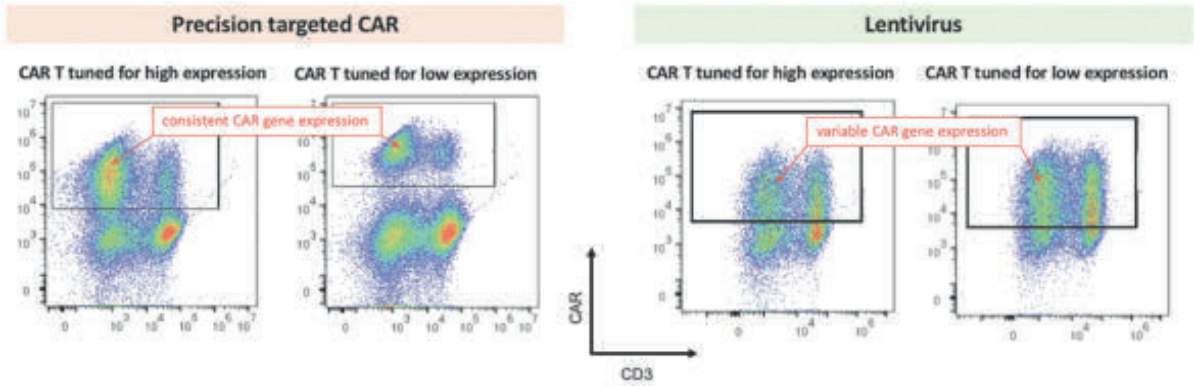


- **Novel co-stimulatory domain.** Our genetically engineered CAR T cells incorporate a novel, proprietary, costimulatory domain called N6, which enables us to enhance cell proliferation and effector function while preserving cell phenotype. We engineered N6 to improve on the function of the 4-1bb costimulatory domain commonly used in autologous CAR T products. Our preclinical data suggests that, compared to 4-1bb, N6 provides an activation signal to the CAR T cells that better preserves cell expansion potential while maintaining naïve cell phenotype following exposure to cancer cells. We also believe N6 can help avoid CAR T cell hyperstimulation, which can contribute to adverse events seen with autologous products.





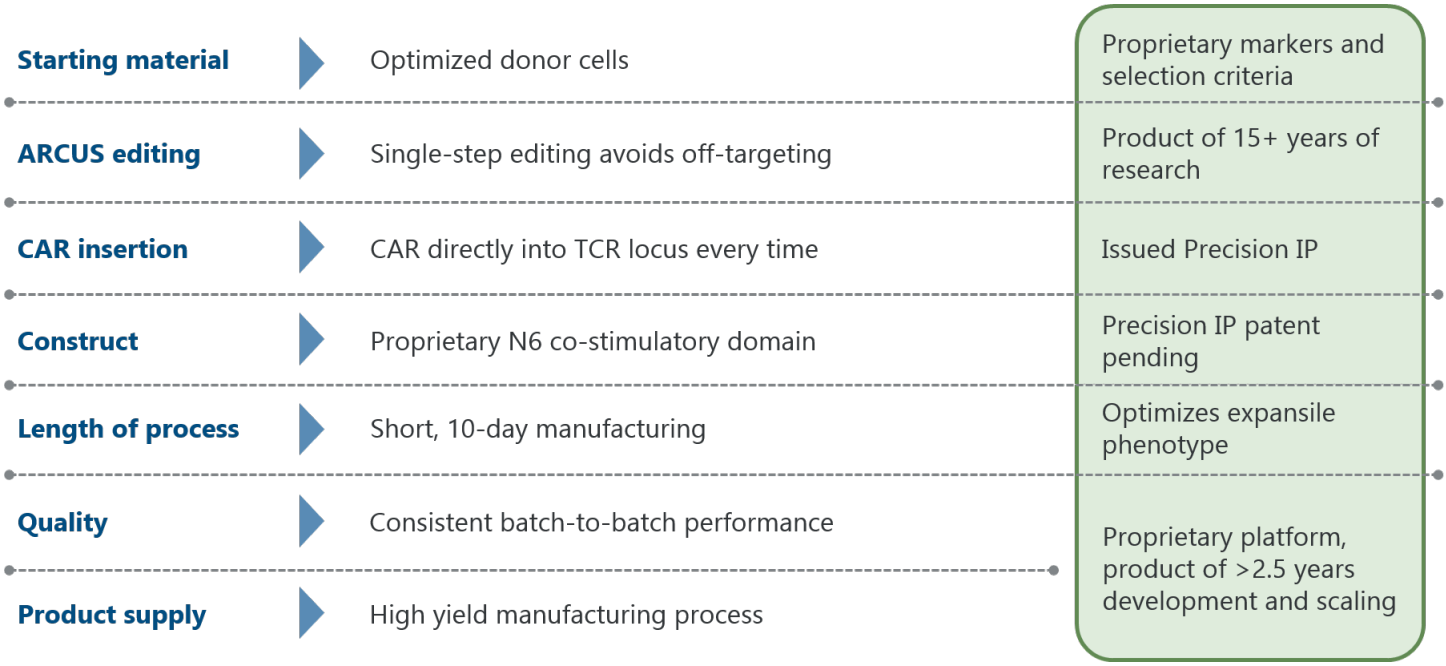
- **Consistency.** By consistently targeting the same insertion of the CAR gene to a defined location in the DNA of the cell, we are able to produce populations of T cells that are identical at the DNA level. This makes the cells in our CAR T cell drug formulation less heterogeneous as compared to manufacturing processes that use lentiviral vectors. Importantly, our genome editing process gives us greater control over the amount of CAR that is expressed on the surface of each CAR T cell, which determines how easily the CAR T cell is activated once it encounters a cancer cell. This allows us to "fine-tune" the CAR T cells to ensure that they respond appropriately to the cancer but do not become hyper-activated or exhausted. The below comparison demonstrates the difference in consistency achieved by using lentivirus delivery compared with targeted delivery through an ARCUS nuclease. CAR T cells produced using ARCUS exhibit reduced cell-to-cell variability as well as more controlled levels of CAR gene expression depending on whether the cells are tuned for high expression or low expression.



- **Scalability.** To realize the potential benefits of allogeneic CAR T cell therapy, it will be important to manufacture as many cells as possible in each batch in accordance with GMP. Scaling efficiently requires scale-up at every step in the process and, as with all drug manufacturing, process development takes significant time and capital. In July 2019, we opened our MCAT facility, which we believe is the first in-house cGMP compliant manufacturing facility dedicated to genome-edited, off-the-shelf CAR T cell therapy product candidates in the United States. We made the decision early in the development of our CAR T cell platform to invest in process development and manufacturing rather than initiating clinical trials with a process that would not fully support development and commercialization. We did this, in part, because we believed that several attributes of ARCUS, such as high specificity and high knock-in efficiency, would allow us to scale manufacturing more effectively than our competitors. As a consequence of our early investment and the one-step editing method enabled by ARCUS, we have scaled our manufacturing process today, adding in-house capabilities through the opening of our MCAT

facility. Over the last twelve months, we have manufactured our lead anti-CD19 allogeneic CAR T cell product candidate at a multi-billion cell scale consistently.

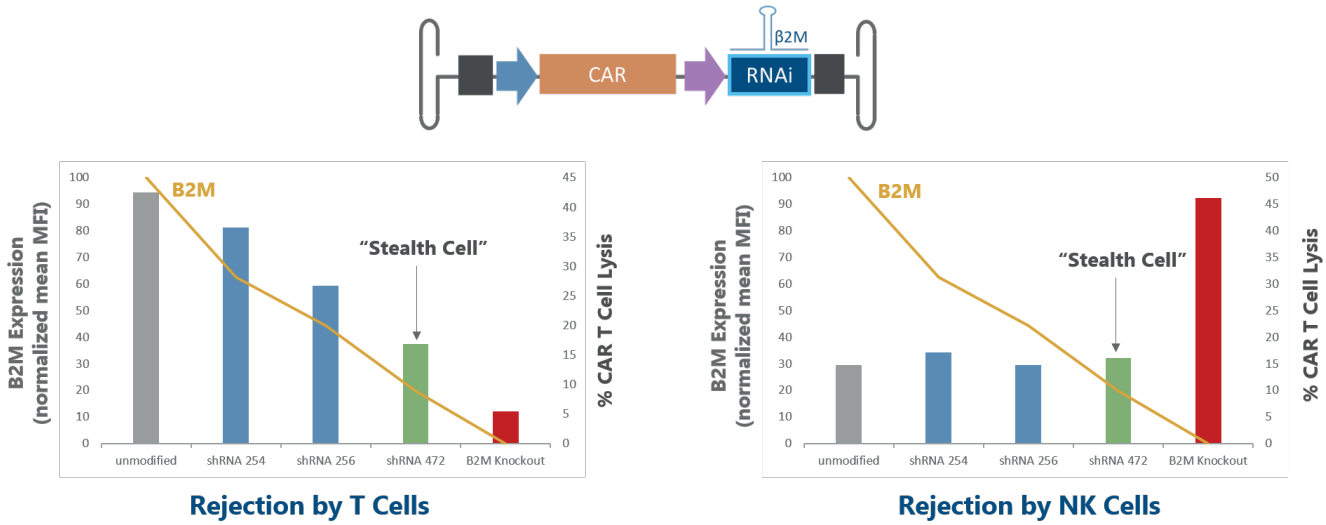
Key features of Precision's allogeneic CAR T platform



Preventing CAR T Cell Rejection

A patient's immune system is expected to recognize allogeneic CAR T cells as foreign and destroy or reject the cells. This rejection could limit the efficacy of the CAR T therapy if the cells do not persist long enough in the patient to eradicate the tumor. Patients who receive CAR T therapy are typically preconditioned prior to being given the cell therapy using lymphodepleting drugs such as cyclophosphamide or fludarabine, which suppress the immune system of the patient. We believe that this degree of preconditioning will be sufficient to prevent CAR T cell rejection by patients who receive our treatments due to our unique approach to producing CAR T cells. Our CAR T production process preserves T cell phenotypes that we believe are highly expansile *in vivo* and therefore do not require an aggressive lymphodepletion regime to survive and proliferate in the body.

Our ongoing Phase 1/2a clinical trial of PBCAR0191 employs a standard lymphodepletion regimen comprised of cyclophosphamide at a dose of 1,500mg/m^2 over three days and fludarabine at a dose of 90mg/m^2 over three days. Based on the initial clinical data from this trial, we believe this lymphodepletion regime to be effective given the high quality of our cell product. However, higher concentrations of fludarabine and cyclophosphamide have been delivered safely to patients. Therefore, we also have the option to increase or decrease the dose of lymphodepletion in the future to further optimize CAR T cell persistence and clinical efficacy if needed, and we will evaluate the need for this based on the assessment of clinical data from our ongoing trials. In addition, we have the ability to incorporate a novel piece of our technology that we call "stealth cell" into the CAR T product candidate. The stealth cell technology is a modified CAR T vector that is designed to suppress a gene called beta-2-microglobulin, or B2M, in CAR T cells using a short-hairpin RNA, or shRNA. B2M is a component of the major histocompatibility complex type 1, a cell surface receptor which activates T cells. In preclinical studies, we and others have observed that suppression or elimination of B2M reduces the rejection of CAR T cells by T cells from an unrelated individual. However, we have found that complete elimination of B2M, for example by knocking the gene out using gene editing, provokes rejection of the CAR T cells by an alternative immune cell called natural killer, or NK cells. As shown in the figure below, in preclinical studies, we have observed that suppression of B2M to a level that is approximately 5% to 20% of normal levels can significantly reduce rejection by T cells without inducing an NK response.



Our Allogeneic CAR T Immunotherapy Pipeline

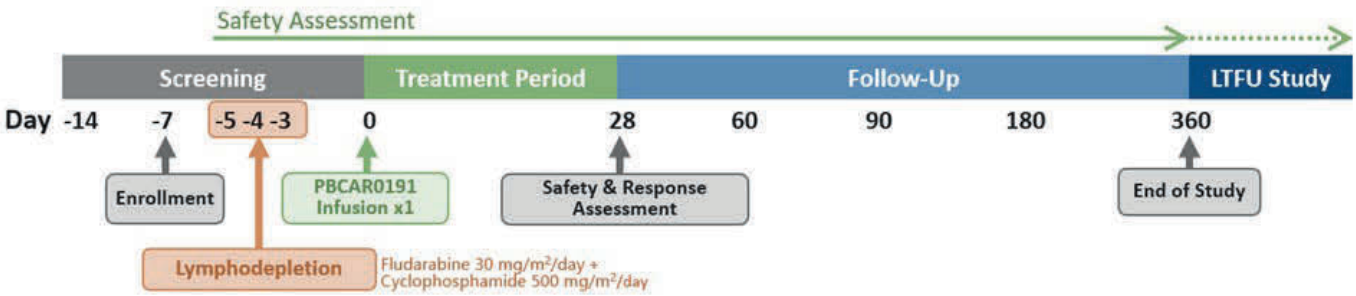
We are leveraging our CAR T cell platform to develop product candidates against validated CAR T cell targets. By focusing on validated targets, we seek to avoid many technical hurdles associated with early clinical development and can validate our allogeneic platform in patients with fewer variables. This approach also allows us to leverage the abundance of available public resources for these targets, including CARs, cell and animal models, and clinical protocols. We believe that our modular CAR T platform will allow us to leverage proof-of-concept from our ongoing and planned initial human trials for multiple other CAR T programs. We believe that we have developed the first allogeneic CAR T cell platform capable of producing drug product at scale, with a potentially optimal cell profile for therapeutic efficacy and true off-the-shelf delivery without the need for harsh and potentially toxic lymphodepletion. We believe that the combination of these factors, along with our next generation ARCUS technology, puts us in a differentiated position to become the leader in the development of allogeneic CAR T therapies.

In December 2019, we reported initial data from the first six patients with advanced NHL and the first three patients with advanced ALL treated with PBCAR0191 at the lowest two dose levels from our ongoing Phase 1/2a clinical trial. These initial data indicated no serious adverse events or dose-limiting toxicities, and demonstrated initial evidence of cell-mediated anti-tumor activity. As of December 31, 2019, dosing of patients at the third dose level was underway.

The first three product candidates in our allogeneic CAR T cell development pipeline are:

- **PBCAR0191**. We are developing PBCAR0191, an allogeneic anti-CD19 CAR T cell product candidate for the treatment of adult R/R NHL and adult R/R B-cell precursor ALL. CD19 is a protein that is expressed on the surface of B cells. It is a well-validated target for CAR T cell therapy and the two currently marketed autologous CAR T cell therapy products also target CD19. In February 2016, we entered into the Servier Agreement, pursuant to which we have agreed to develop allogeneic CAR T cell therapies for CD19.

We are currently evaluating patients in a Phase 1/2a clinical trial of PBCAR0191 in adult patients with R/R NHL or R/R B-cell precursor ALL, the trial design of which is shown in the figure below. The primary objective of this trial is to evaluate the safety and tolerability of PBCAR0191, as well as to determine the maximum tolerated dose. Secondary objectives include evaluating the anti-tumor activity of PBCAR0191. We are also evaluating the expansion, trafficking and persistence of PBCAR0191 in this trial. NHL and ALL cohorts are evaluated independently. The base trial design includes up to three dose levels: 3.0 x 10^5 cells/kg, 1.0 x 10^6 cells/kg and 3.0 x 10^6 cells/kg. Patients will be further evaluated for a follow-up period of 11 months. The trial is being conducted at the following four clinical sites across the United States: Moffitt Cancer Center in Florida, City of Hope Cancer Treatment and Research Center in California, Dana-Farber Cancer Institute in Massachusetts and MD Anderson Cancer Center in Texas. A further eight to ten sites are expected to be initiated during the course of 2020.



Initial Data from Phase 1/2a Trial of PBCAR0191 in R/R NHL and R/R B-ALL

In December 2019, we announced initial data from our ongoing Phase 1/2a clinical trial of PBCAR0191 in adult patients with R/R NHL or R/R B-ALL. A total of nine patients were reported in these initial Phase 1 trial results, including six with NHL (three treated at Dose Level 1, or DL1, and three treated at Dose Level 2, or DL2), and three with B-ALL (all treated at DL2).

Patients treated at Dose Level 1 (3x10^5 cells/kg) included three NHL patients, two with diffuse large B cell lymphoma and one with mantle cell lymphoma, with a mean age of 54 years (min-max 34-64 years). Patients had received a median of four prior lines of therapy, with two patients being refractory to their last treatment, and one having previously relapsed following treatment with Yescarta®, an FDA-approved autologous CD19-targeted CAR T therapy. Dose Level 2 (1x10^6 cells/kg) included three NHL patients, all with mantle cell lymphoma, with a mean age of 74 years (min-max 71-77 years) who had received a median of two prior lines of therapy, with one patient refractory to their last treatment and two who had relapsed. Three B-ALL patients were also treated at DL2, with a mean age of 56 years (min-max 48-72 years); these patients had received a median of four prior lines of therapy – all three patients were refractory to their last treatment, with two patients having poor prognostic indicators at trial entry.

Patients received a single infusion of PBCAR0191 on day 0, following three days of lymphodepletion using fludarabine 30mg/m^2/day and cyclophosphamide 500mg/m^2/day. The primary objective of this Phase 1 portion of the ongoing Phase 1/2a trial is to evaluate safety as measured by the occurrence of dose limiting toxicities. Secondary objectives include assessment of objective tumor responses using standard criteria, and further evaluation of adverse events, or AEs, and adverse events of special interest, including GvHD, cytokine release syndrome, or CRS, and immune effector cell-associated neurotoxicity syndrome, or ICANS. Data were presented as of a November 4, 2019 cutoff date, with additional critical data collected through December 2, 2019, including occurrence of CRS, ICANS, GvHD and evaluation of objective responses.

Safety of PBCAR0191

No serious adverse events or evidence of GvHD were observed through December 2, 2019. Three of the nine patients treated with PBCAR0191, or 33%, developed CRS including two Grade 1 cases and one Grade 2 case. One of the nine patients, or 11%, developed Grade 2 neurotoxicity. All events of CRS and neurotoxicity resolved, and no deaths occurred on study. In addition, one patient experienced a Grade 3 AE that was deemed related to PBCAR0191 (pain at the site of the patient's tumor mass for one day following infusion) and one patient experienced Grade 4 lymphopenia for a duration of seven days and deemed related to PBCAR0191.

Clinical activity of PBCAR0191

Of the nine patients treated with PBCAR0191, seven, or 78%, had objective evidence of tumor shrinkage at any time point. The data also provided preliminary evidence of dose-dependent CAR T cell expansion and persistence. In the NHL cohort, four of six patients, or 67%, achieved an objective response by Lugano 2014 criteria at day 28+, including three partial responses (two patients treated at DL1 and one patient treated at DL2) and one complete response (patient treated at DL2). As of December 2, 2019, one patient (treated at DL2) remained in complete response. One patient (treated at DL1) achieved a partial response then progressed six months after treatment with PBCAR0191. This was notable given the patient had relapsed following treatment with Yescarta®. The remaining two NHL patients, one treated at DL1 and one at DL2, achieved early responses (one CR, one PR respectively) at day 14; both patients had evidence of disease progression at day 28. In the B-ALL cohort treated at DL2, one of three patients, or 33%, achieved a complete response by the National Comprehensive Cancer Network 2017 criteria at day 28+, with undetectable B-ALL in the bone marrow by flow cytometry, described as minimal residual disease (MRD) negative. The remaining two patients did not respond at day 28; these patients had poor prognostic indicators on entry into the trial: one with prior CNS involvement and 95% blast infiltration into the bone marrow, and one with 77% blast infiltration into the bone marrow and disease refractory to two previous lines of treatment.

CAR T cell expansion and persistence in the peripheral blood was assessed at DL1 and DL2 by flow cytometry and quantitative polymerase chain reaction, or qPCR. Evidence of a dose-dependent increase in cell expansion was observed between subjects treated at DL1 and DL2, as was a dose-dependent increase in CAR T cell persistence. B-cell aplasia and serum cytokine analysis also anecdotally corresponded to observed clinical responses and CAR T cell expansion.

As of December 31, 2019, dosing of patients at Dose Level 3 ($3x10^6$ cells/kg) was underway.

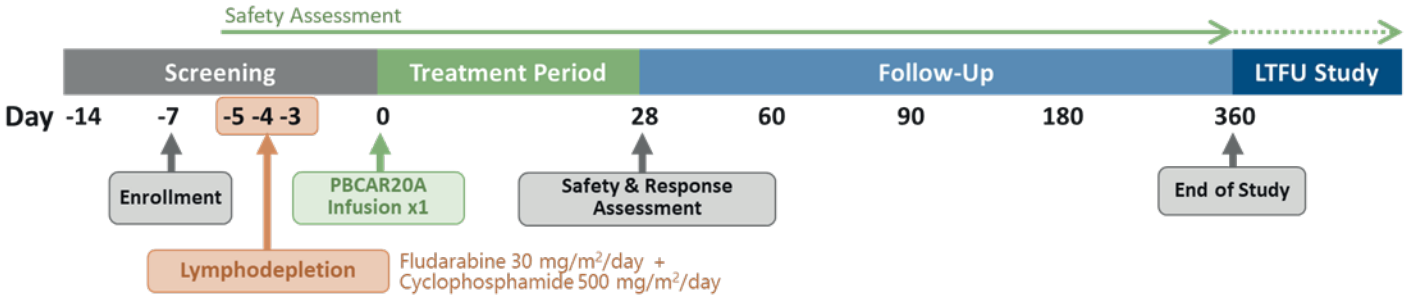
Recent trial amendment

Based on the safety profile and clinical activity observed at DL1 and DL2, we filed a protocol amendment for this trial with the FDA in December 2019. Following feedback from FDA in late January 2020, the protocol amendment is now being implemented. The amended trial design is intended to specifically address key clinical questions. These include assessing the impact of higher total doses of cells on clinical activity and/or the impact of modified lymphodepletion on the ability to achieve durable clinical benefit with associated CAR T cell expansion and persistence. The most important modification is the inclusion of two additional dose levels: Dose Level 4 ($6x10^6$ cells/kg) and Dose Level 5 ($9x10^6$ cells/kg). These higher doses will employ a split dosing strategy following a single lymphodepletion with the intention of optimizing clinical activity while preserving a favorable safety profile. Dose Level 4 will comprise two infusions of $3x10^6$ cells/kg, and Dose Level 5 will comprise three such infusions – this strategy will enable us to explore higher total doses of PBCAR0191 while limiting potential GvHD risk. In addition, we have introduced a modification to allow for the option to increase or decrease the doses of fludarabine and cyclophosphamide used in the lymphodepletion protocol if data suggest that CAR T cell rejection limits efficacy. The final modification allows for the option to re-dose patients with PBCAR0191 following evidence of clinical response but with subsequent disease progression.

We expect to present updated results from this trial during the course of 2020.

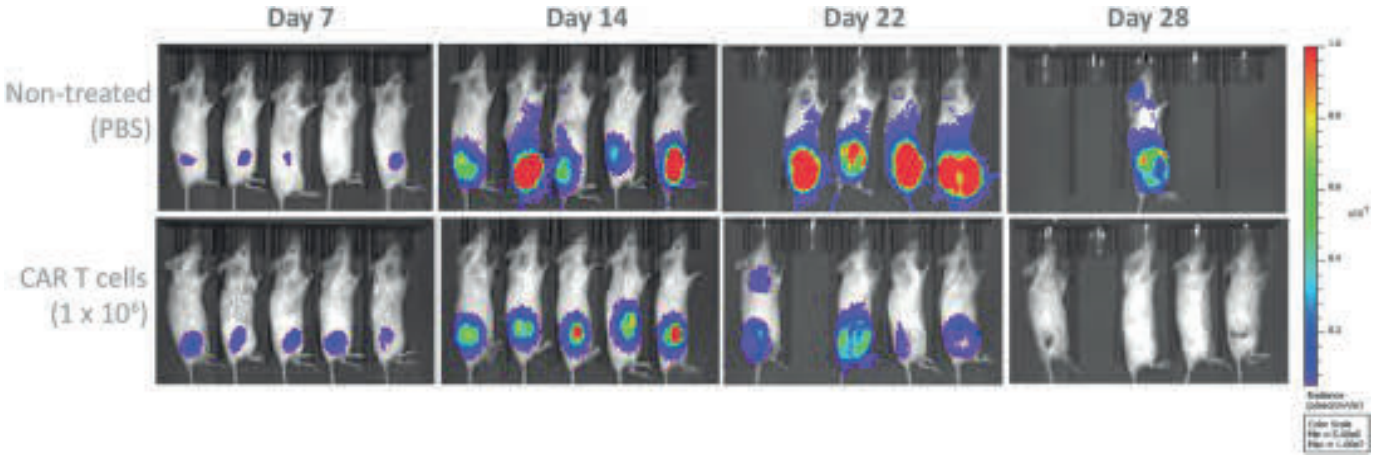
PBCAR20A. Our second allogeneic CAR T therapy candidate is PBCAR20A, an allogeneic anti-CD20 CAR T cell product candidate for the treatment of NHL, chronic lymphocytic leukemia, or CLL, and small lymphocytic lymphoma, or SLL. Like CD19, CD20 is a protein expressed on the surface of B cells. It is a validated target for cancer treatment and several CD20-targeted therapies, such as the monoclonal antibody Rituxan, have long histories of clinical and commercial success. In September 2019, the FDA cleared our IND application for PBCAR20A and we expect to commence a Phase 1/2a clinical trial for PBCAR20A in the first quarter of 2020. It will be investigated in subjects in two cohorts: NHL and CLL/SLL. The trial will include patients with NHL, of which a subset will have the diagnosis of mantle cell lymphoma, or MCL. We have received Orphan Drug Designation for the treatment of MCL.

In our planned Phase 1/2a clinical trial, the primary objective will be to evaluate the safety and tolerability of PBCAR20A, as well as to determine the maximum tolerated dose. Secondary objectives will include evaluating the anti-tumor activity of PBCAR20A. We also plan to evaluate the expansion, trafficking and persistence of PBCAR20A in this trial. Based on the adverse events observed to date with PBCAR0191, the FDA has agreed to allow us to commence dosing with PBCAR20A directly at Dose Level 2, which we expect to accelerate the timing for our expected completion of the trial. We therefore currently plan to investigate two dose levels in this trial, 1.0 x 10^6 cells/kg and 3.0 x 10^6 cells/kg. Our clinical plan for this trial is depicted in the graphic below:



Our accepted IND for PBCAR20A included data from our preclinical study in mice measuring cell proliferation, cytotoxic killing, and production of effector cytokines in response to co-culture with CD20+ or CD20- target cells. PBCAR20A CAR T cells were observed to proliferate in response to stimulation by CD20+ K20 cells (K562 myelogenous leukemia cells transfected to express human CD20) at a wide range of doses (effector to target ratios ranging from 1:1 to 1:9). These observations show that, in this study, PBCAR20A cells became activated by and killed CD20+ cells at a wide range of cell doses. In this study, we observed that PBCAR20A cells did not proliferate in response to co-culture with CD20 negative cell K562 cells.

We also evaluated the potency of PBCAR20A *in vivo*. As shown below, PBCAR20A was observed to prolong survival in a mouse model of lymphoma (Raji Sub-Q model) at both doses tested (1.0 x 10^6 and 5.0 x 10^6 cells per mouse), which we believe supports further development. PBCAR20A was observed to be well-tolerated in this study.

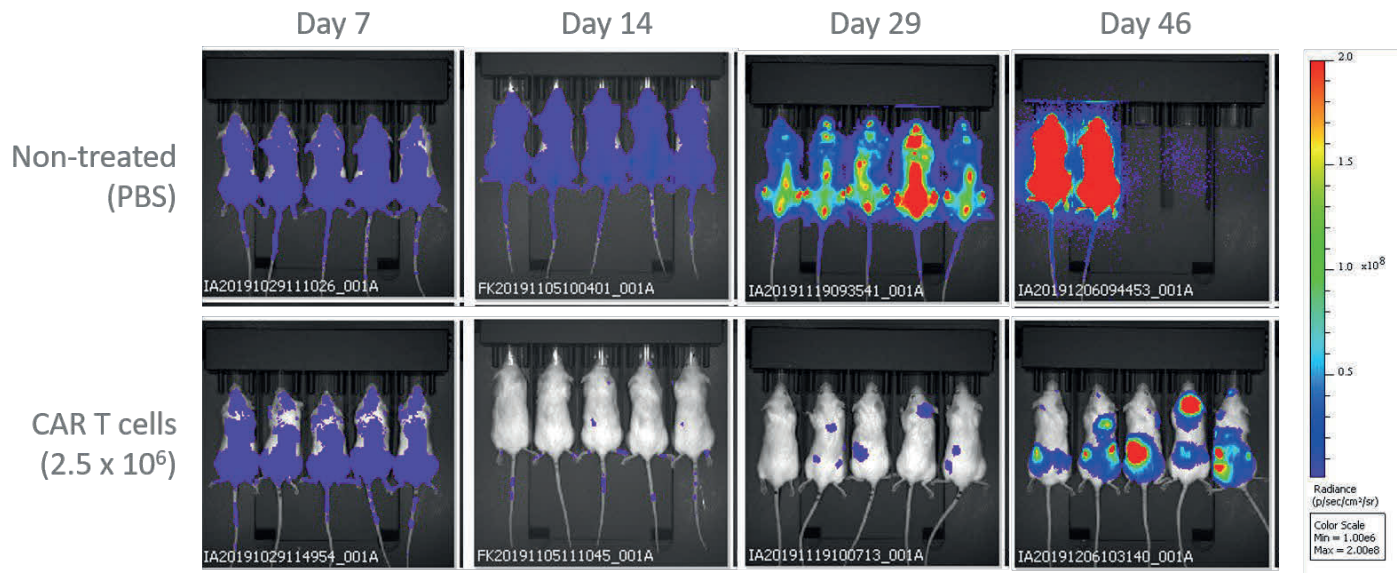


PBCAR269A. We are developing PBCAR269A as an allogeneic anti-BCMA CAR T cell product candidate for the treatment of R/R multiple myeloma. BCMA is a protein that is expressed on the surface of mature B cells called "plasma cells" that are responsible for the disease and is a validated CAR T cell target. In January 2020, the FDA cleared our IND for PBCAR269A.

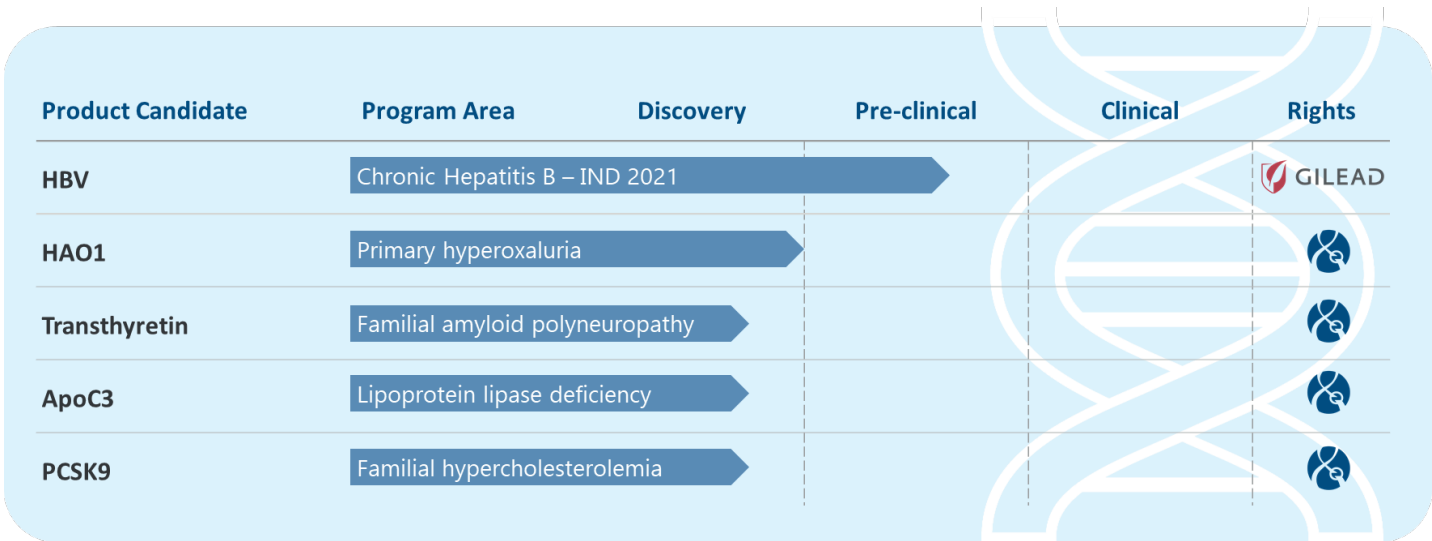
We plan to commence a Phase 1/2a open-label, multi-center, dose-escalation clinical trial in patients with R/R multiple myeloma in 2020. In this trial, the primary objective will be to evaluate the safety and tolerability of PBCAR269A, as well as to determine the maximum tolerated dose. Secondary objectives will include evaluating the anti-tumor activity of PBCAR269A. We also plan to evaluate the expansion, trafficking and persistence of PBCAR269A in this trial. We expect to investigate up to three dose levels: 6.0 x 10^5 cells/kg, 2.0 x 10^6 cells/kg and 6.0 x 10^6 cells/kg.

We evaluated the potency of PBCAR269A CAR T cells in a preclinical study in mice by measuring cell proliferation, cytotoxic killing and production of effector cytokines in response to co-culture with BCMA+ or BCMA- target cells. In this study, PBCAR269A CAR T cells were observed to proliferate in response to stimulation by BCMA+ target cells including MM.1S (a human multiple myeloma cell line) and KBCMA (K562 myelogenous leukemia cells transfected to express human BCMA) at a wide range of doses (effector to target ratios ranging from 1:1 to 1:8). These observations show that, in this study, PBCAR269A cells became activated by and killed BCMA+ cells at a wide range of cell doses. We further observed that PBCAR269A cells did not proliferate in response to co-culture with BCMA- K562 cells.

We also evaluated the potency of PBCAR269A *in vivo*. As shown below, PBCAR269A was observed to prolong survival in a mouse model of multiple myeloma, which we believe supports further development. PBCAR269A was observed to be well-tolerated in this study.



Our *in vivo* Gene Correction Platform



Overview

We expect *in vivo* genome editing to be a significant focus of our operations long-term because the differentiated attributes of ARCUS are particularly advantageous for this type of application. *In vivo* gene correction involves the delivery of ARCUS nucleases directly into a patient's cells to treat disease at the level of the underlying DNA. *In vivo* genome editing is more complex and challenging than *ex vivo* approaches like CAR T cells due to the need to safely deliver ARCUS directly to cells in the body. We believe that *in vivo* applications are particularly well suited to ARCUS because they require extremely low levels of off-target editing and efficient delivery.

Due to the demands of *in vivo* editing, we are taking a highly disciplined approach to managing our project portfolio that emphasizes studies in large animals, using both viral and non-viral delivery technologies. We believe that there is a remarkable lack of large animal data in the genome editing field and that demonstrating safety and efficacy in large animals is an important gating step prior to beginning human clinical studies. Thus, we are advancing an extensive and diverse portfolio of programs toward *in vivo* efficacy and toxicity studies and are generating a large animal dataset that, we believe, will be the most comprehensive of any in the field. Our two most advanced programs in this area are focused on chronic hepatitis B, in partnership with Gilead, and PH1 which is wholly owned by Precision.

Treatment of Genetic Disease

Genetic diseases are caused by errors in the DNA that lead to misfunction of a cell or tissue. While the underlying cause of a particular genetic disease can often be complex and variable, DNA errors generally fall into two categories: loss-of-function or gain-of-function. Genetic diseases are most frequently caused by loss-of-function errors in which a particular gene is mutated at the DNA level in such a way that it is either non-functional or less functional than it should be. In these cases, treating the disease requires *adding* the function that the cell or tissue is otherwise lacking. Gain of function genetic disorders are the result of DNA errors that cause a gene to acquire a new, harmful function that leads to disease. In these cases, it is necessary to remove the unwanted function to treat the disorder.

Genetic disease is a very active area of therapeutic development, and the therapies that are available or in development are, to a large extent, as variable and specialized as the diseases themselves. There are, however, two gene therapy platform approaches that are being broadly applied to the treatment of multiple genetic disorders. For the treatment of loss-of-function diseases, AAV-based gene therapy can often be an effective treatment. AAV is a non-integrating virus that can be used to deliver DNA to a wide range of different cell types in a patient. The virus can be engineered to deliver a functional copy of a gene that is otherwise missing or under-performing in the cell. This approach can, in some cases, restore normal function to the cell and alleviate the symptoms of the disease.

While a number of AAV-based gene therapies appear to be showing great promise in clinical trials, the approach is subject to a number of limitations. Many patients have antibodies in their blood that recognize and inactivate the AAV virus before it can deliver the DNA into the patient's cells. In addition, among patients who do *not* have antibodies upon initial treatment with the virus, most will develop antibodies following the first dose. Therefore, in most cases, it is only possible to dose a patient one time. Most importantly, although AAV-based gene therapy can be an effective treatment, it is probably not a permanent *cure* because AAV-delivered genes do not generally persist for more than a few years in the body. While the duration of virus persistence varies from cell-to-cell and from patient-to-patient, it is not believed to be permanent and symptoms of the disease can return once the virus is no longer present in the body.

Our Approach to in vivo Gene Correction

Our goal is to cure genetic diseases by correcting the DNA errors responsible for causing them. In principle, *in vivo* genome editing can likely be used to cure any genetic disorder. In practice, however, *in vivo* genome editing is limited by several challenges that, we believe, are best addressed using ARCUS:

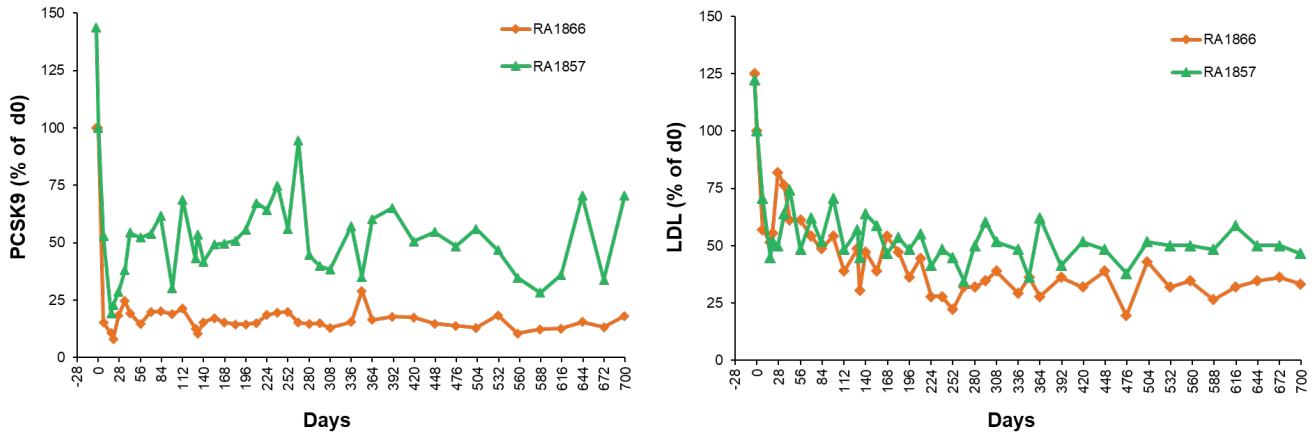
- **Specificity.** *In vivo* genome editing requires an extremely high degree of precision to minimize the occurrence of any unwanted off-target editing. Off-target changes to the DNA could, potentially, have significant safety implications that may not manifest themselves until well after administration of the therapy. As described above, we believe that the differentiated attributes of ARCUS enable us to create endonucleases that have a high degree of specificity and minimal levels of off-target editing to address this significant safety concern.

- **Delivery.** Gene therapy delivery technologies suitable for the delivery of genome editing tools to tissues *in vivo* have not been developed for all tissues. Delivery challenges are particularly pronounced for editing applications that require promoting DNA repair by HDR because it is necessary to deliver both the nuclease and the DNA "donor" template for HDR. We have focused our initial development efforts on genetic disorders of the liver and eye, two tissues for which we believe we have good options for delivery and in which we have shown ARCUS to be effective in preclinical studies. We believe the small size of our ARCUS nucleases and their ability to efficiently promote HDR will enable us to address a greater variety of genetic diseases requiring more complex delivery strategies.

- **Efficiency.** Genome editing efficiency is a critical parameter for *in vivo* therapeutic efficacy because the requisite edit must be achieved in a sufficient number of cells to have therapeutic benefit. Efficiency is best measured *in vivo* in animals because it is affected by multiple parameters including delivery, endonuclease activity and the accessibility of the DNA target site in the organism. Moreover, we believe that only large animals such as non-human primates accurately model these different parameters and are representative of the human condition. As such, we have placed significant emphasis on large animal studies and have demonstrated, we believe, therapeutic levels of editing efficiency using ARCUS in the most relevant models. This gives us greater confidence that ARCUS will translate from the lab bench to the clinic.

The potential of ARCUS for *in vivo* genome editing is highlighted in a July 2018 publication in *Nature Biotechnology* that describes a research project performed as part of a sponsored research collaboration between our company and Dr. Jim Wilson's Orphan Disease Center at the University of Pennsylvania. Co-authors of the publication include Derek Jantz and Jeff Smith, two of our co-founders. This publication is, to our knowledge, the first peer-reviewed publication of *in vivo* genome editing data in non-human primates. We reported well-tolerated, long-term, high-efficiency editing of the PCSK9 gene in non-human primates using ARCUS. A single IV administration of an AAV vector encoding a PCSK9-specific ARCUS nuclease was able to efficiently knock out the gene in the livers of Rhesus macaques, a species of monkey, resulting in up to approximately 85% reduced levels of PCSK9 protein in the blood. This reduction in PCSK9 then resulted in significantly reduced levels of LDL-C, commonly known as "bad cholesterol," in the blood of treated animals. Because this therapeutic effect is due to modifications to the DNA itself, the benefit of the treatment appeared to be permanent. The first animals that were treated have maintained reduced levels of PCSK9 and LDL-C since they were treated in February 2017. Importantly, even at the highest dose the treatment was observed to be well tolerated in the study. These peer reviewed data exemplify the power of ARCUS for *in vivo* editing at therapeutically meaningful levels of efficiency.

PCSK9 and LDL Serum Levels

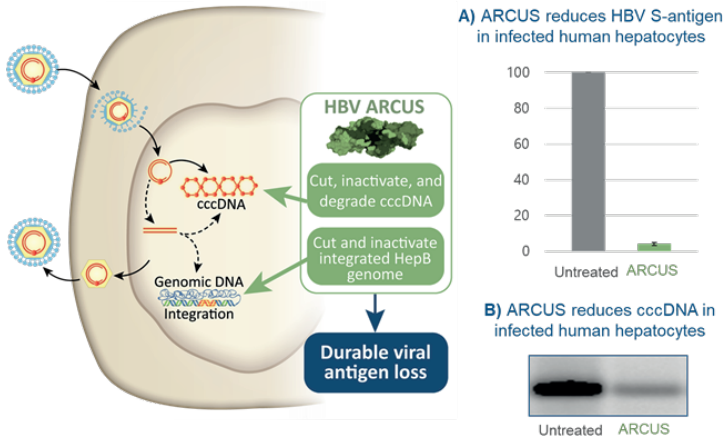


We believe that establishing collaborations with other groups that have additive domain expertise and access to the most relevant animal models will be important to advancing our *in vivo* gene correction platform, and we have entered into a number of collaborations and licensing agreements with third parties to help us advance our *in vivo* editing portfolio.

Hepatitis B Program

In September 2018, we entered into a collaboration and license agreement with Gilead to co-develop an ARCUS-based treatment for chronic hepatitis B infection. Infection by the hepatitis B virus, or HBV, is in many ways analogous to a gain-of-function genetic disorder. In this case, the deleterious DNA that needs to be eliminated is the genome of the virus itself. To this end, we are collaborating with Gilead to develop an ARCUS-based product candidate that is designed to specifically target and eliminate both forms of viral DNA (integrated DNA and covalently closed circular DNA ("cccDNA")) from infected liver cells. Our ARCUS-based product candidate is designed to cut and thereby inactivate or degrade cccDNA and to cut and thereby inactivate the integrated hepatitis B genome. We believe making these edits gives us the ability to permanently eliminate the chronic viral infection, and potentially cure the disease. Submission of an IND for this product candidate is currently targeted for 2021.

In preclinical studies, we developed a pair of ARCUS nucleases that recognized and cut conserved DNA sequences in the Hepatitis B genome. We observed that these nucleases reduced HBV S-antigen and cccDNA HBV-infected primary human hepatocytes, as shown below.



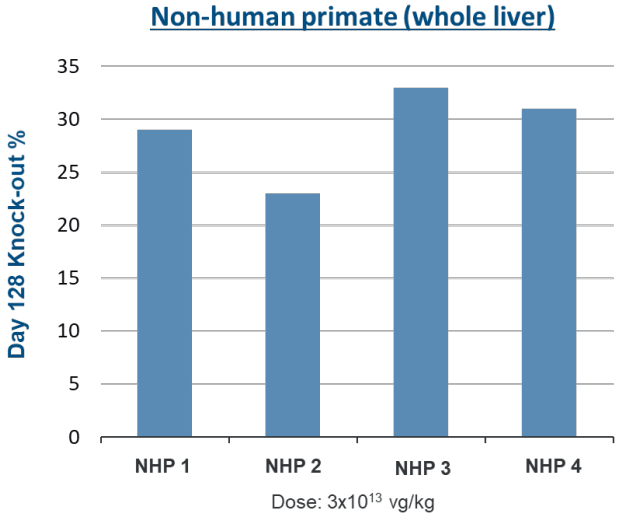
Primary Hyperoxaluria Type 1 (PH1) Program

In January 2020, we announced that we will advance a program designed to target the rare genetic disease PH1 as our lead wholly owned *in vivo* gene correction program. PH1 affects approximately 1-3 people per million in the United States and is caused by loss of function mutations in the AGXT gene. This gene encodes an enzyme which is involved in the production of the amino acid glycine in the liver. In patients with PH1 who lack this enzyme, crystals of calcium oxalate form in the kidneys leading to painful kidney stones which may ultimately lead to renal failure. Approximately 40% of PH1 patients are found to have already progressed to end stage renal disease at the point of diagnosis, requiring a combined liver-kidney transplant.

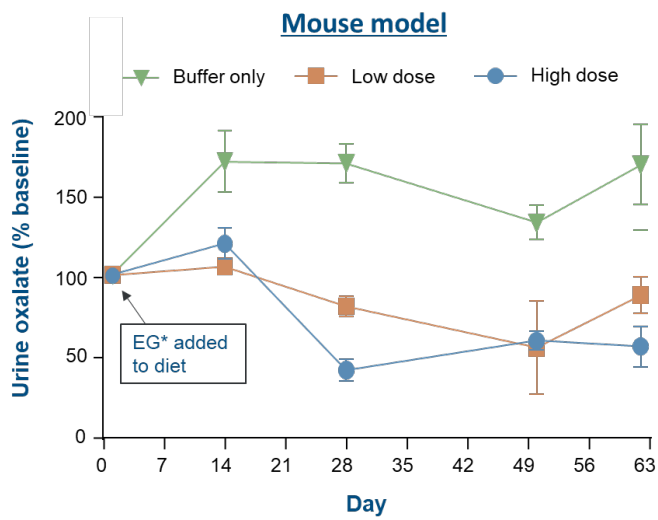
Using ARCUS, we are developing a potential therapeutic approach to PH1 that involves knocking out a gene called HAO1 which acts upstream of AGXT. Suppressing HAO1 has been shown in preclinical models to prevent the formation of calcium oxalate. We therefore believe that a one-time administration of an ARCUS nuclease targeting HAO1 may be a viable strategy for a durable treatment of PH1 patients.

In preclinical studies we have demonstrated that ARCUS efficiently knocked out the HAO1 gene in non-human primates. We have also demonstrated in a mouse model of PH1 that administration of an ARCUS nuclease targeting HAO1 resulted in approximately 70% reduction in urine calcium oxalate levels. We plan to select a clinical candidate for this program during 2020.

ARCUS efficiently knocked-out the *HAO1* gene in non-human primates following AAV8 delivery

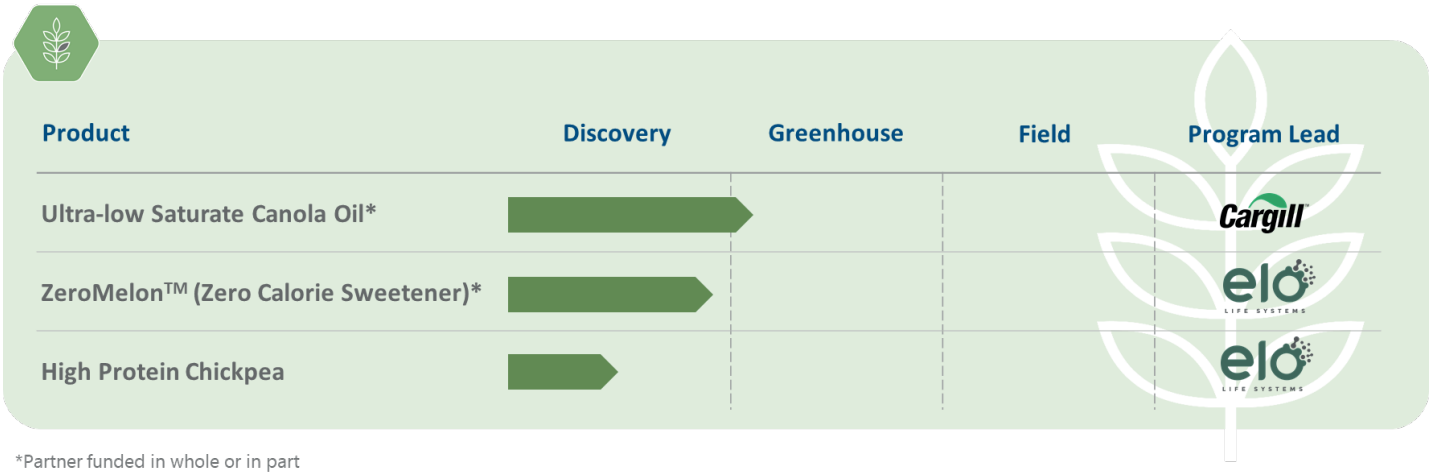


ARCUS treatment resulted in ~70% reduction in urine oxalate in a PH1 mouse model



*Ethylene glycol

Our Food Platform



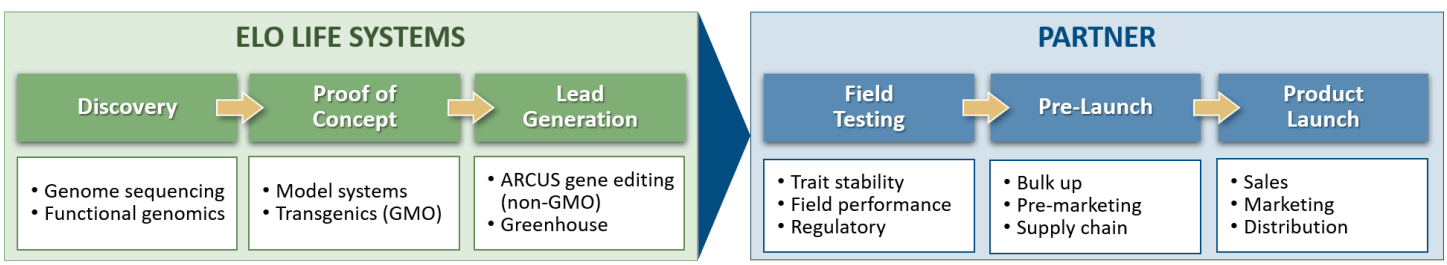
*Partner funded in whole or in part

Technology-Centric Solutions to Meet Changing Demands in Food and Agriculture

The total global food and agriculture market, estimated to be worth $5 trillion (2015), is heavily influenced by the availability of critical raw material ingredients and changing consumer behavior. With the global population projected to reach 8.5 billion by 2030, demand for basic food and nutrition needs has already put a lot of pressure on traditional food production systems. In response, the food and agriculture industry is currently in the process of a slow, but massive, repositioning effort to reinvent its capital-intensive infrastructure, complex business structures and product pipelines. This is creating new opportunities to disrupt the otherwise archaic food industry by introducing technology solutions that address unmet needs. Of particular concern to the industry is the agronomic impact of climate change. Many staple foods and critical ingredients, such as citrus, bananas and coffee, are under threat from environmental changes and the new pathogens it can bring. The food and agriculture industry has also seen significant shifts in consumer preferences in which consumers are actively transitioning to high quality and healthier foods and beverages, while rejecting artificial ingredients, sugar and salt, creating a demand for natural and holistic ingredients built on a sustainable supply chain. Traditional approaches to agricultural innovation are slow, siloed, rely heavily on non-scalable academic advancements and continue to use inefficient crop improvement practices. We believe that many of the current pressures on the food and agriculture industry from climate-related threats and changing consumer preferences can be effectively addressed using biotechnology. However, consumers are generally opposed to genetically modified organisms, or GMOs, which makes food companies reluctant to incorporate them into their products. Our wholly-owned food and agriculture focused subsidiary, Elo Life Systems, was created to help food companies "thread the needle" between competing pressures to improve the genetics of their ingredients while avoiding the incorporation of GMO organisms.

Elo Life Systems: Innovation-Focused Technology Platform and Business Model

Elo Life Systems is our wholly owned subsidiary, dedicated to addressing the needs of consumers and consumer-facing industries in the food and agriculture sector. Our business model is heavily partner-focused. In the food and agriculture industry, timelines to market are long and the field is dominated by a relatively small number of entrenched companies. Therefore, it is a very difficult to bring a product to market without a larger partner. Thus, we seek partnerships early in the product development process to optimize our chances of market success. Under this partnership model, we are responsible for the early phases of the project, starting from concept through production of a "lead," which is typically a gene edited plant that has the desired trait in greenhouse testing and is ready for scale-up and testing in the field. At that point, our partners typically assume responsibility for subsequent development and commercialization. Because large consumer-facing food companies are often not directly responsible for producing their own starting ingredients, this transfer may involve an intermediate in the supply chain such as a seed producer or grower who is responsible for pre-commercial activities. Whenever possible, we try to partner with the entire supply chain early in the project to ensure a smooth transition across phases of development. In general, our partners are responsible for financing all or a portion of our development costs, which greatly reduces our capital requirements. We are then generally eligible to share in revenues derived from successfully commercialized products developed under these partnerships.



Elo's Technology Platform

Our end-to-end food platform is built to support rapid innovation across multiple crop species. With the ARCUS genome editing platform as our cornerstone technology, we have integrated complementary tools and technologies both upstream and downstream to potentially be a complete solutions provider.

At the core of our food platform is our ARCUS editing technology. We are one of the first to apply genome editing technology to crop plants and we believe we have the most in-depth experience in crop genome editing in the industry. Over the last decade, we have developed highly efficient methods to improve delivery and functionality of ARCUS nucleases in plants to edit DNA. These nucleases have been successfully validated in collaborative projects with major food and agriculture companies like Cargill, BASF, Bayer CropScience and DuPont Pioneer Hi-bred. Importantly, ARCUS can be used to create small deletions or insertions in plants using a non-plant pest- or pathogen-based delivery approach. As such, we believe that many of the food and agriculture product candidates we may develop have the potential to obtain nonregulated status in the United States and other territories and thereby avoid GMO labels. This aspect of the technology platform is critical to food producers, particularly as they respond to consumer demands for healthier products. Because Elo partners with large companies that generally lack significant biotechnology capabilities, it was necessary for us to build these capabilities in-house to complete Elo's portion of the development process. This end-to-end platform is unusual in the industry and, we believe, makes Elo an attractive partner. In addition to ARCUS, Elo's in-house capabilities include:

- **Genomics.** Many of the most attractive opportunities for Elo involve emerging and under-studied crops, such as stevia and monk fruit. We have integrated genome sequencing and bioinformatic platforms in-house in order to identify the genome sequence of plants, enabling us to identify targets for editing with ARCUS nucleases.

- **Target discovery and validation.** Our informatics platform is built on principles of machine learning that allow us to synthesize, sequence and phenotype information from both public and internal datasets to correlate genome sequence with plant characteristics. This allows us to identify genetic targets for ARCUS editing that are predicted to yield a desired phenotype. These targets can then be validated in specific crops and at least partially validated in model systems such as tobacco and Arabidopsis using different molecular approaches such as editing or RNAi.

- **Multi-crop transformation.** Most of the crops of interest to Elo and our partners do not have established transformation protocols and are not readily amenable to gene editing. To this end, we have developed a sophisticated collection of plant transformation vectors and protocols over the last decade that allow us to rapidly develop gene-edited variants of otherwise intractable species. This technology allows us to overcome what is otherwise a significant barrier to entry into a new crop species.

- **Plant growth infrastructure.** Elo has a dedicated facility and capabilities of cultivating gene edited plants from incubator to greenhouse.

Ultra-low saturated fatty acid canola oil (in collaboration with Cargill Inc.)

Canola oil is the third largest vegetable oil by volume after palm and soybean oil. In the United States, canola oil is one of the most widely consumed oils, second only to soybean oil. With worldwide production at 30 million metric tons in 2017, global canola oil is estimated to be a $20 billion industry.

Cargill is one of the world's largest growers and processors of canola. Since 2014, Elo and Cargill are engaged in a collaboration to produce ARCUS-optimized canola varieties and have achieved significantly lower levels (less than 4.5%) of saturated fatty acids compared to the current levels (7%) in greenhouse studies. This oil with the desirable premium trait is intended for the quick-service restaurants and food ingredients industries, and products made with it—particularly fried foods—may be able to use front-of-package nutrient content claims on saturated fat levels, such as "Low in Saturated Fat" or "No Saturated Fat," depending on their overall nutritional profile.

This program has generated canola varieties with up to an approximately 33% decrease in total saturated fats compared to un-edited varieties in greenhouse studies and we have not observed any less desirable traits in these canola varieties in these greenhouse studies to date.

ZeroMelon™ Low-Calorie Sweeteners from Watermelon

Low calorie sweeteners are a rapidly growing segment of the food and beverage industry as companies respond to consumer demands for low-sugar snack foods and soda alternatives. Based on an April 2019 report by Mordor Intelligence, the global food sweetener market is estimated to be worth approximately $82 billion by 2024. In addition, the adoption of "sugar taxes" by many cities across the United States and Europe are significantly impacting profit margins and creating an acute need for alternatives to cane sugar and corn syrup such as the natural, high intensity sweeteners in stevia and monk fruit.

We believe that a potentially optimal low calorie sweetener comes from monk fruit. The monk fruit compound mogroside V is approximately 250 times sweeter than cane sugar and contains zero calories, making it an excellent potential alternative to cane sugar and stevia. However, monk fruit currently is not scalable for large scale applications in the food and beverage industry as a result of lower productivity and a lack of reliable supply chain. We are currently collaborating with an industry partner to develop a watermelon variety to produce this high value metabolite in a crop that is readily cultivated across North America and Europe.

We are now focused on moving this program forward towards initiation of greenhouse trials.

Plant-Based Proteins

Shifting consumer preferences across the globe towards higher protein diets has created unprecedented demand for plant-based protein sources. We do not believe that this demand for plant-based proteins, projected to grow to a $10.5 billion global industry by 2020, can be met without the application of biotechnology to increase protein content in different crop species.

In 2018, we launched Elo Life Systems Australia, a subsidiary of Elo that will support research programs in Australia. Elo Life Systems Australia's primary focus is developing climate-resilient legumes with improved protein and nutritional profiles, starting with chickpea. We aim for the resulting products to make a significant contribution towards the increasing demand for sustainable plant-based proteins as a healthful alternative to animal protein.

Manufacturing

We believe that we have strong internal scientific process development and manufacturing capabilities, including our Manufacturing Center for Advanced Therapeutics, or MCAT, an in-house cGMP compliant manufacturing facility supporting our therapeutic product development platforms which we opened in 2019. We believe that MCAT is the first in-house cGMP compliant manufacturing facility in the United States dedicated to genome-edited, off-the-shelf CAR T cell therapy products. We believe that having internal manufacturing capacity and expertise is a competitive advantage that enables enhanced control over process development timelines, costs and intellectual property.

We have leased approximately 33,600 square feet of space for our MCAT facility at a location approximately seven miles from our headquarters in Durham, North Carolina. We have a modular, three-suite cleanroom setup, for CAR T cell, mRNA and AAV production, to process development for our allogeneic CAR T immunotherapy platform. Our manufacturing facility leverages single-use, disposable, closed-system operations aligned to our technology platforms to ensure both flexibility and cost effectiveness. The initial scope is creating clinical trial material for certain of our planned clinical trials in 2020. In the longer term, we believe MCAT has the potential to be a commercial launch facility.

We currently contract with third parties for the manufacturing of materials used in the production of our product candidates. To date, our third-party manufacturers have met our manufacturing requirements. We believe that there are alternate sources of supply that can satisfy our requirements.

The manufacturing process for our allogeneic CAR T immunotherapy platform utilizes a one-step cell engineering method in which a CAR gene is targeted directly into the T cell receptor alpha constant, or TRAC, locus. We believe this approach greatly streamlines the manufacturing process and have entered into a license agreement with a principal supplier for research and clinical licensed technology used in such process. Commercial raw materials and reagents for this production are readily available. Our manufacturing strategy for our *in vivo* gene correction platform and our food platform is to internally control process development and manufacturing to safeguard the proprietary nature of our technology and facilitate our ability to function as an integrated life sciences company.

License and Collaboration Agreements

Servier

In February 2016, we entered into the Servier Agreement as subsequently amended, with predecessor entities of Servier. Pursuant to this agreement, we have agreed to develop allogeneic chimeric antigen receptor T cell therapies for up to six unique antigen targets, the first of which was selected at the inception of the agreement. Upon selection of an antigen target, we perform early-stage research and development on individual T cell modifications for the selected target, develop the resulting therapeutic product candidates through Phase 1 clinical trials and manufacture clinical trial material for use in Phase 2 clinical trials.

We received an upfront payment of $105.0 million under the Servier Agreement. At Phase 2 readiness for any product candidate covered by the Servier Agreement, Servier may exercise a commercial option to proceed with development and commercialization of the product candidate, subject to option fees. Following the exercise of any such commercial option, Servier must use commercially reasonable efforts to develop and commercialize the product candidate. We have the ability to receive total payments, including the upfront payment, option fees and milestone payments, in the aggregate across all six targets that may be selected, of up to approximately $1.6 billion. This includes up to $1.5 billion in milestone payments, consisting of up to $401.3 million in development milestone payments and up to $1.1 billion in commercial milestone payments. We are also entitled to receive tiered royalties ranging from the mid-single digit percentages to sub-teen percentages on worldwide net sales of any products developed under the Servier Agreement, subject to customary potential reductions. Servier's obligation to pay royalties to us expires on a country-by-country and licensed product-by-licensed product basis upon the latest of (1) the expiration of the last to expire valid claim of all Precision patents covering a licensed product, (2) expiration of all regulatory exclusivity with respect to a licensed product in the applicable country of sale, and (3) the expiration of 10 years following the first commercial sale of such licensed product in such country. We also have the right to participate in the development and commercialization of any licensed products resulting from the collaboration through a 50/50 co-development and co-promotion option in the United States, subject to our payment of an option fee, which is exercisable after Servier's commercial option exercise. So long as Servier holds a commercial license with respect to any particular licensed product, we may not develop, manufacture or commercialize any engineered human T cells with chimeric antigen receptors for use in humans directed to the same antigen target as the target of that licensed product.

Unless terminated earlier, the Servier Agreement expires upon the first to occur of (1) the expiration of the period in which Servier may nominate antigen targets, if there are no included targets under the agreement, (2) the expiration of the period in which Servier may exercise a commercial option on a licensed product candidate, if no commercial options have been exercised by Servier, or (3) the expiration of the last to expire royalty term for the licensed products and satisfaction of all of Servier's payment obligations under the agreement. Servier has the right to terminate the agreement for convenience, either in its entirety or on a target-by-target or product-by-product basis, by providing advance notice to us. We may terminate immediately upon notice to Servier if Servier (itself or through the use of certain affiliates or a third party) or any sublicensee initiates or participates in a patent challenge against our patents licensed by Servier under the agreement. In addition, the Servier Agreement may be terminated (a) by either party for the other party's material breach that remains uncured as specified in the agreement, (b) by either party upon the occurrence of certain insolvency-related events of the other party and (c) upon mutual agreement of the parties in the event either party suffers an event of force majeure as specified in the agreement. If Servier terminates the agreement for our uncured material breach of provisions in the agreement that restrict development, manufacture or commercialization of engineered human T cells with chimeric antigen receptors for use in humans directed to a target selected by Servier, certain licenses we grant to Servier will become royalty-free, fully paid-up, perpetual and irrevocable with respect to the licensed product candidates and licensed products directed to the target that was the subject of such breach, and Servier will be deemed to have previously exercised its commercial option for any then-existing licensed product candidates directed to such target.

Gilead

In September 2018, we entered into the Gilead Agreement to develop genome editing tools using ARCUS to target viral DNA associated with the Hepatitis B virus. Pursuant to the terms of the agreement, Gilead received an exclusive license to exploit the resulting synthetic nucleases and products that use them to treat the Hepatitis B virus in humans, and we are entitled to receive up to approximately $40 million in research funding over an initial three year term and milestone payments of up to an aggregate of $445 million, consisting of up to $105.0 million in development milestone payments and up to $340.0 million in commercial milestone payments. We are also entitled to receive tiered royalties ranging from the high single digit percentages to the mid-teen percentages on worldwide net sales of the products developed through the term of the agreement, subject to customary potential reductions. Gilead's obligation to pay royalties to us expires on a country-by-country and licensed product-by-licensed product basis, upon the latest to occur of certain events related to expiration of applicable patents, expiration of regulatory exclusivity or 10 years following the first commercial sale of the first licensed product in such country.

Unless terminated earlier, the Gilead Agreement will continue, on a licensed-product-by-licensed-product and country-by-country basis until the expiration of a defined royalty term for each licensed product and country. Gilead has the right to terminate the Gilead Agreement for convenience by providing advance notice to us as specified in the Gilead Agreement. Gilead may also terminate the agreement during the collaboration term if we enter into certain change of control transactions with a third party that is clinically developing or commercializing products in the field of the Hepatitis B virus. In addition, either party may terminate the Gilead Agreement (1) for material breach by the other party and a failure to cure such breach within the time period specified in the Gilead Agreement and (2) upon the occurrence of certain insolvency-related events of the other party.

Duke University

In April 2006, we entered into the Duke License, pursuant to which Duke University ("Duke") granted us an exclusive (subject to certain non-commercial rights reserved by Duke), sublicensable, worldwide license under certain patents related to certain meganucleases and methods of making such meganucleases owned by Duke to develop, manufacture, use and commercialize products and processes that are covered by such patents, in all fields and in all applications. The patents that we license pursuant to the Duke License have been generated through the use of U.S. government funding and are therefore subject to certain federal regulations. See Part I, Item 1A. "Risk Factors— Risks Related to Intellectual Property—Some of our in-licensed intellectual property has been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies, and compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers."

Under the Duke License, in addition to upfront licensing fees, we are also required to pay Duke (1) a total of $0.3 million in milestone payments, a portion of which we paid upon the completion of our Series A financing, a further portion of which we paid upon our first signed partnership in excess of $1 million, and the remainder of which we will be required to pay upon successful commercialization of seed traits and human therapeutics, (2) royalties in the low single digit percentages on net sales of licensed products and licensed processes sold by us and our affiliates, subject to certain reductions in certain circumstances, with certain annual minimum royalties, and (3) certain percentages of sublicensing revenue received under sublicenses granted to third parties, which are creditable against annual minimum royalties and are subject to certain reductions in certain circumstances. For sublicenses of non-commercial products, the percentage of sublicensing revenue payable to Duke is in the mid-teen percentages for sublicense revenues owed from royalties received and low double-digits for sublicense revenues owed from non-royalty payments. For sublicenses of commercial products created by us and derivatives thereof, the percentage is determined by the highest negotiated royalty rate in such sublicense. If the highest negotiated royalty rate between us and our sublicensee exceeds a mid-single digit percentage, the percentage of sublicensing revenue payable to Duke will be high single digit, decreasing to low single digit as the highest negotiated royalty rate in such sublicense increases. The Duke License will expire upon the expiration of the last-to-expire patent that is licensed to us. We may terminate the Duke License by providing advance written notice as specified in the Duke License. Either party may terminate the Duke License in the event of the other party's uncured material breach or for the other party's fraud, willful misconduct or illegal conduct with respect to the subject matter of the Duke License.

Cellectis S.A.

In January 2014, we entered into a cross-license agreement with Cellectis S.A., which we refer to as the Cellectis License, in connection with a settlement of litigation matters (1) between Cellectis and us and (2) among Cellectis, Duke and us. Cellectis granted us a non-exclusive, sublicensable, worldwide, fully paid, royalty-free license to certain modified I-CreI homing endonuclease patents and Cellectis patents asserted in the litigation, to make, use and commercialize modified I-CreI homing nucleases and products developed using such nucleases, in all fields. The license we received from Cellectis is subject to the rights of a preexisting license agreement that Cellectis entered into with a third party, and the license granted to us excludes any rights exclusively granted by Cellectis under such preexisting license, which preexisting license is limited to certain specific applications unrelated to the fields of human therapeutics and plant agriculture, for so long as the rights under the preexisting license remain exclusive.

We granted Cellectis a non-exclusive, sublicensable, worldwide, fully paid-up, royalty-free license to certain modified I CreI homing endonuclease patents and our patents asserted in the litigation matters (1) between Cellectis and us and (2) among Cellectis, Duke and us to make, use and commercialize modified I-CreI homing nucleases and products developing using such nucleases, in all fields except those for which we did not receive rights from Cellectis due to the preexisting license.

The Cellectis License will expire upon the expiration of the last-to-expire valid claim of all of the patents licensed to or from each of the parties to the agreement. Either party may terminate any of the licenses granted under the agreement (1) in the event of the other party's material breach, subject to an opportunity to cure within the time period specified in the Cellectis License, or (2) if the other party directly or indirectly challenges a patent licensed to it by the other party.

Competition

As a diversified life sciences company, we compete in multiple different fields. The biotechnology, pharmaceutical and agricultural biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on intellectual property and proprietary products. We principally compete with others developing and utilizing genome editing technology in the human health and plant sciences sectors, including companies such as Allogene Therapeutics, Inc. Cellectis S.A., CRISPR Therapeutics, AG, Editas Medicine, Inc., Intellia Therapeutics, Inc., Sangamo Therapeutics, Inc, and Beam Therapeutics, Inc.

We compete with many biotechnology and pharmaceutical companies, academic research institutions, governmental agencies and public and private research institutions. We expect that our operations focused on CAR T cell product candidate development and commercialization will face substantial competition from those focusing on immunotherapy solutions. Several companies, including Novartis Pharmaceuticals Corp. and Gilead have obtained FDA approval for autologous cell therapies, and a number of companies, including Cellectis S.A., Celgene Corp., Allogene Therapeutics and CRISPR Therapeutics AG, are pursuing allogeneic cell therapies. We expect that our operations focused on developing products for *in vivo* treatment of genetic disease will face substantial competition from others focusing on gene therapy treatments, especially those that may focus on conditions that our product candidates target. Moreover, any human therapeutics products that we may develop will compete with existing standards of care for the diseases and conditions that our product candidates target and other types of treatments, such as small molecule, antibody or protein therapies.

Many of our current or potential competitors in the therapeutics space, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials and marketing approved products than we do. In addition to competing on the bases of safety, efficacy, timing of development and commercialization, convenience, cost, availability of reimbursement and rate of adoption of potential product candidates, we may also compete with these competitors in recruiting and retaining qualified personnel, establishing clinical sites, establishing relationships with collaborators or other third parties, registering patients for clinical trials and acquiring technologies complementary to, or necessary for, our product development platforms. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

We also compete with participants in the agricultural biotechnology space, including Pairwise Plants, LLC, Caribou Biosciences, Inc., Corteva Agriscience, Tropic Biosciences UK LTD, Calyxt, Inc. and Cibus. Competition for improving plant genetics comes from conventional and advanced plant breeding techniques, as well as from the development of genetically modified traits. Competition for providing more nutritious ingredients for food companies comes from chemical-based ingredients, additives and substitutes, which are developed by various companies. We also face less direct competition from trait research and development companies and agricultural research universities and institutions. We compete with respect to many aspects of the product development cycle in the plant sciences space, such as computational capabilities for identifying relevant gene targets, access to germplasm and enabling technologies and entry into strategic relationships to facilitate product development and commercialization.

Many of our current or potential competitors in the agricultural biotechnology space, either alone or with others, have significantly greater financial resources and expertise in research and development, manufacturing, testing and marketing approved products than we do. Mergers and acquisitions in the plant science, specialty food ingredient and agricultural biotechnology, seed and chemical industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through strategic relationships with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, as well as in acquiring technologies complementary to, or necessary for, our food platform.

Furthermore, we rely upon a combination of patents and trade secret protection, as well as license and confidentiality agreements to protect the intellectual property related to our proprietary technologies, product candidate development programs and product candidates. Our success depends in large part on our ability to secure and maintain patent protection in the United States and other countries with respect to the ARCUS nucleases used in our existing allogeneic CAR T immunotherapy, *in vivo* gene correction and food programs, as well as any future product candidates. Moreover, the industries in which we operate are characterized by the existence of large numbers of patents and frequent allegations of patent infringement. If, therefore, we are unable to obtain and maintain patent protection for our technology and product candidates, or if the scope of the patent protection obtained or in-licensed is not sufficiently broad or if the validity of such patent protection is threatened, we may not be able to compete effectively, as it could create opportunities for competitors to enter the market or dissuade other companies from collaborating with us to develop products and technology, any of which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved.

Intellectual property

Our success depends in part on our abilities to (1) obtain and maintain proprietary protection for ARCUS, (2) defend and enforce our intellectual property rights, in particular, our patent rights, (3) preserve the confidentiality of our know-how and trade secrets, and (4) operate without infringing valid and enforceable intellectual property rights of others. We seek to protect our proprietary position by, among other things, exclusively licensing U.S. and certain foreign patent applications, and filing U.S. and certain foreign patent applications related to ARCUS, existing and planned programs, and improvements that are important to the development of our business. We also rely on trademarks, trade secrets, know-how, continuing technological innovation and confidential information, and

the pursuit of licensing opportunities, to develop and maintain our proprietary position and protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and others who may have access to proprietary information, under which they are bound to assign to us inventions made during the term of their employment or term of service. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

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

Our patent portfolio consists of a combination of issued patents and pending patent applications that are owned by us or licensed by us from third parties. As of December 31, 2019, we have an exclusive license from Duke under 12 issued U.S. patents and two pending U.S. patent applications. In addition, as of December 31, 2019, we own 18 issued U.S. patents, 20 pending non-provisional U.S. patent applications, and eight pending PCT international patent applications. We also exclusively license from Duke or own many corresponding patents and patent applications outside the United States, as described below. We intend to pursue, when possible, additional patent protection, including composition of matter, method of use and process claims, related to ARCUS. We also intend to obtain rights to existing delivery technologies through one or more licenses from third parties.

ARCUS Platform Patent Families

We license one patent family from Duke and own three patent families that are directed to the core technologies employed in our ARCUS platform for nuclease design. Thus, each of our product candidates is protected by one or more patents in these families.

The first family, licensed from Duke, includes 12 issued U.S. patents, eight issued European patents, three issued Japanese patents, and one issued patent in each of Australia and Canada. This family also includes one pending patent application in the United States and one pending patent application in each of Europe, Japan and Canada. Patents in this family include claims directed to (1) recombinant meganucleases having altered cleavage specificity, altered heterodimer formation, and/or altered DNA binding affinity, (2) methods for cleaving target recognition sites in DNA using such meganucleases, and (3) methods for producing genetically modified eukaryotic cells using such meganucleases. Patents in this family have a standard expiration date of October 18, 2026, subject to potential extensions.

The second family, which we own, includes four issued U.S. patents, three issued patents in Europe, two issued patents in Japan, and one issued patent in Australia. This family also includes one pending patent application in each of the United States, Europe, Japan and Australia. Patents in this family include claims directed to (1) recombinant single-chain meganucleases, and (2) methods for producing isolated genetically modified eukaryotic cells using such meganucleases. Patents in this family have a standard expiration date of October 31, 2028, subject to potential extensions.

The third family, which we own, includes three issued patents in the United States, and two issued patents in each of Europe and Australia. This family also includes one pending patent application in each of the United States and Europe. Patents in this family include claims directed to methods of cleaving DNA at specific four base pair sites using a recombinant meganuclease. Patents in this family have a standard expiration date of July 14, 2029, subject to potential extensions.

The fourth family, which we own, includes two pending provisional patent applications in the United States. Patent applications in this family include claims directed to recombinant meganucleases engineered to cleave recognition sequences having specific four base pair sites. Patents in this family, if issued, will likely have a standard expiration date of May 7, 2040, subject to potential extensions.

Immunotherapy Patent Families

We own seventeen patent families that are directed to immunotherapy, including CAR T cell therapies. Some of these are applicable to immunotherapies and/or CAR T cells directed to killing a variety of different types of infected or cancerous cells. Others are directed to specific indications in which cells expressing particular antigens are targeted. Each of our immunotherapy product candidates is protected by one or more patents in these families.

The first family includes nine issued U.S. patents, and pending patent applications in each of the United States, Europe, Australia, Canada, China, Hong Kong, Israel, Japan, Mexico and South Korea. Patents in this family include claims directed to (1) populations of genetically modified human T cells in which 20%-65% of the cells have reduced expression of an endogenous TCR and express an anti-cancer antigen CAR from DNA inserted into the cells' TCR alpha constant region (TRAC) gene, (2) methods for using such populations of genetically modified human T cells for cancer immunotherapy, (3) pharmaceutical compositions comprising such populations of genetically modified human T cells, (4) genetically modified human T cells which have reduced expression of an endogenous TCR and express an anti-cancer antigen CAR from DNA inserted into the cells' TRAC gene, (5) methods for using such genetically modified human T cells for cancer immunotherapy, and (6) pharmaceutical compositions comprising such genetically modified human T cells. Patents in this family have a standard expiration date of October 5, 2036, subject to potential extensions.

The second family includes one issued patent in Europe and pending patent applications in each of the United States, Europe, Australia, Canada and Japan. Patent applications in this family include claims directed to (1) first-generation recombinant meganucleases that cleave a target in the TRAC gene, (2) nucleic acids and vectors encoding such recombinant meganucleases, (3) methods for producing genetically modified eukaryotic cells, including CAR T cells, using such meganucleases, and (4) methods of using such genetically modified eukaryotic cells for cancer immunotherapy. Patents in this family will have a standard expiration date of October 5, 2036, subject to potential extensions.

The third family includes a pending PCT international patent application. That PCT patent application includes claims directed to (1) second-generation engineered meganucleases that cleave a specific target in the TRAC gene, (2) nucleic acids and vectors encoding such recombinant meganucleases, (3) methods for producing genetically modified eukaryotic cells, including CAR T cells, using such meganucleases, (4) genetically modified eukaryotic cells or populations of cells prepared by such methods, (5) pharmaceutical compositions comprising such cells or populations of cells, and (6) methods of treating diseases using such cells, populations of cells or pharmaceutical compositions to treat diseases, including cancer immunotherapy. Patents in this family, if issued, will likely have a standard expiration date of April 11, 2039, subject to potential extensions.

The fourth family includes pending patent applications in the United States, Europe, Australia, Canada and Japan. Patent applications in this family include claims directed to (1) nucleic acids encoding co-stimulatory domains having certain amino acid sequences, (2) recombinant DNA constructs and vectors comprising such nucleic acids, (3) nucleic acids and vectors encoding such recombinant meganucleases, (4) genetically modified cells comprising such nucleic acids, (5) methods for producing such genetically modified cells, (6) pharmaceutical compositions comprising such cells, and (7) methods of immunotherapy using such cells. Patents in this family, if issued, will have a standard expiration date of October 4, 2037, subject to potential extensions.

The fifth family includes pending patent applications in the United States and Europe. Patent applications in this family include claims directed to (1) methods of reducing cytotoxicity associated with DNA transfection in primary eukaryotic cells, (2) methods for increasing the number of gene-edited primary eukaryotic cells following DNA transfection, (3) methods for increasing gene editing frequency in primary eukaryotic cells following DNA transfection, (4) methods for increasing the number of primary eukaryotic cells comprising targeted insertion of an exogenous sequence of interest into the genome following DNA transfection, (5) methods for increasing insertion frequency of an exogenous sequence of interest into the genome in primary eukaryotic cells following DNA transfection, (6) methods for high throughput screening of primary human T cells expressing a CAR or exogenous TCR, (7) methods for high throughput screening of primary human T cells expressing a CAR or exogenous TCR, and (8) genetically modified primary eukaryotic cells produced by such methods. Patents in this family, if issued, will likely have a standard expiration date of April 30, 2038, subject to potential extensions.

The sixth family includes pending patent applications in the United States, Europe, Australia, Canada and Japan. Patent applications in this family include claims directed to (1) recombinant meganucleases that recognize and cleave a recognition sequence within the human beta-2-microglobulin gene, (2) nucleic acids and vectors encoding such recombinant meganucleases, (3) methods for producing genetically modified eukaryotic cells, including CAR T cells, using such meganucleases, (4) populations of genetically modified eukaryotic cells in which 80% of the cells have reduced expression of an endogenous TCR and 80% of the cells have reduced expression of beta-2-microglobulin, (5) pharmaceutical compositions comprising such populations of genetically modified eukaryotic cells, and (6) methods for using such genetically modified eukaryotic cells for cancer immunotherapy. Patents in this family, if issued, will have a standard expiration date of December 22, 2036, subject to potential extensions.

The seventh family includes a pending PCT international patent application and pending patent applications in the United States, Europe, Australia, Canada and Japan. Patent applications in this family include claims directed to (1) nucleic acids encoding an engineered antigen receptor (e.g., a CAR) and an inhibitory molecule (e.g., an RNA interfering with beta-2-microglobulin expression), (2) genetically modified eukaryotic cells comprising such nucleic acids, (3) methods for producing such genetically modified eukaryotic cells using such nucleic acids and an engineered nuclease that promotes insertion of such nucleic acids, (4) genetically modified eukaryotic cells expressing an engineered antigen receptor and having expression of beta-2-microglobulin or MHC Class I molecules reduced by 10%-95%, (5) pharmaceutical compositions comprising such genetically modified eukaryotic cells, and (6) methods for using such genetically modified eukaryotic cells for immunotherapy. Patents in this family, if issued, will likely have a standard expiration date of May 8, 2038, subject to potential extensions.

The eighth family includes a pending PCT international patent application and pending patent applications in the United States, Europe, Australia, Canada and Japan. Patent applications in this family include claims directed to (1) engineered meganucleases that recognize and cleave a recognition sequence in an upstream intron of the human TRAC gene, (2) nucleic acids and vectors encoding such engineered meganucleases, (3) methods for producing genetically modified T cells using such nucleic acids or vectors, (4) genetically modified T cells in which an exogenous sequence is inserted into an upstream intron of the human TRAC gene and endogenous TCR expression is reduced, (5) populations of such genetically modified T cells, (6) pharmaceutical compositions comprising such genetically modified T cells, and (7) methods of treating disease using such genetically modified T cells and pharmaceutical compositions, including cancer immunotherapy. Patents in this family, if issued, will likely have a standard expiration date of June 27, 2038, subject to potential extensions.

The ninth family includes a pending PCT international patent application. That PCT patent application includes claims directed to (1) nucleic acids and vectors encoding certain modified human epidermal growth factor receptor, or EGFRs, (2) genetically modified cells and populations of cells, including T cells and CAR T cells, expressing such modified EGFRs, (3) methods for producing such genetically modified cells using such nucleic acids or vectors encoding such modified EGFRs, (4) pharmaceutical compositions comprising such genetically modified cells, (5) methods for isolating such genetically modified cells, (6) methods of treating disease using such genetically modified cells and pharmaceutical compositions, including cancer immunotherapy, and (7) methods of depleting such genetically modified cells in a subject using anti-modified EGFR antibodies. Patents in this family, if issued, will likely have a standard expiration date of October 3, 2038, subject to potential extensions.

We own eight additional patent families that include pending provisional patent applications in the United States that are directed to immunotherapies, including CAR T cell therapies, or to technologies that are useful for the manufacture of immunotherapies. We jointly own one patent family that includes a pending provisional patent application in the United States directed to immunotherapies. We will determine in the future whether to pursue each of these applications.

In August 2019, the Patent Trial and Appeal Board (the "PTAB") of the USPTO initiated two patent interferences, administrative proceeding within the USPTO, involving the U.S. patents issued to us in the first family of immunotherapy patents described above and a pending U.S. patent application filed by a third party. An interference is conducted by the PTAB when opposing parties have applied for patent claims to the same invention or substantially the same invention. The interference is conducted to determine which party, if either, is entitled to claims to the subject matter of the interference.

Hepatitis B Virus Gene Therapy Patent Families

We own three patent families that are directed to gene therapy for Hepatitis B virus.

The first family includes pending patent applications in the United States, Europe, Japan, Canada, Australia, China, South Korea, Mexico, Israel, the African Regional Intellectual Property Organization, Brazil, Chile, Colombia, Costa Rica, the Dominican Republic, Egypt, Eurasia, Guatemala, Hong Kong, India, Indonesia, Morocco, Malaysia, New Zealand, Nigeria, Panama, Peru, the Philippines, Saudi Arabia, Singapore, South Africa, Thailand, Ukraine, and Vietnam. Patent applications in this family include claims directed to (1) engineered meganucleases that recognize and cleave recognition sites in the Hepatitis B virus ("HBV") genome, (2) nucleic acids and vectors encoding such engineered meganucleases, (3) pharmaceutical compositions comprising such nucleic acids or meganucleases, and (4) methods for treating HBV infection using such meganucleases, nucleic acids and/or pharmaceutical compositions. Patents in this family, if issued, will have a standard expiration date of October 13, 2037, subject to potential extensions.

The second family includes a pending PCT application and patent applications in the United States, Argentina, Taiwan, and the Gulf Cooperation Council. Patent applications in this family include claims directed to (1) second-generation engineered meganucleases that recognize and cleave recognition sites in the Hepatitis B virus, or HBV genome, (2) nucleic acids and vectors encoding such engineered meganucleases, (3) pharmaceutical compositions comprising such nucleic acids or meganucleases, and (4) methods for treating HBV infection using such meganucleases, nucleic acids and/or pharmaceutical compositions. Patents in this family, if issued, will likely have a standard expiration date of April 11, 2039, or April 12, 2039, subject to potential extensions.

The third family includes a pending provisional application in the United States. That provisional patent application is directed to engineered meganucleases that cleave recognition sequences in the HBV genome. Patents in this family, if issued, will likely have a standard expiration date of December 6, 2040, subject to potential extensions.

Other Patent Families

We own one patent family directed to engineered meganucleases and methods of treatment targeting the PCSK9 gene, which is associated with familial hypercholesterolemia. This family includes a pending PCT international and pending patent applications in the United States, Europe, Australia, Canada, China, Israel, Japan, Mexico, and South Korea. Patents in this family, if issued, will have a standard expiration date of April 20, 2038, subject to potential extensions.

We own two patent families directed to engineered meganucleases and methods of treatment targeting the rhodopsin gene, which is associated with retinitis pigmentosa. The first family includes pending patent applications in the United States, Europe, Australia, Canada and Japan. Patents in this family, if issued, will have a standard expiration date of September 8, 2036, subject to potential extensions. The second family includes a pending provisional patent application in the United States. Patents in this family, if issued, will likely have a standard expiration date of April 11, 2040, subject to potential extensions.

We own two patent families that are directed to engineered meganucleases and methods of treatment targeting the hydroxyacid oxidase 1 gene, which is associated with primary hyperoxaluria 1. The first family includes a pending PCT international application and one pending provisional patent application in the United States. Patents in this family, if issued, will likely have a standard expiration date of December 20, 2039, subject to potential extensions. The second family includes two pending provisional patent applications in the United States. Patents in this family, if issued, will likely have a standard expiration date of March 26, 2040, subject to potential extensions.

We own two patent families that are directed to engineered meganucleases and methods of treatment targeting the Factor VIII gene, which is associated with Hemophilia A. The first family includes pending patent applications in the United States, Europe, Australia, Canada, and Japan. Patents in this family, if issued, will have a standard expiration date of May 3, 2037, subject to potential extensions. The second family includes a pending PCT international patent application. Patents in this family, if issued, will likely have a standard expiration date of November 1, 2038, subject to potential extensions.

We own one patent family directed to engineered meganucleases and methods of treatment targeting the ApoC3 gene, which is associated with diseases resulting from abnormal triglyceride synthesis. This family includes a pending provisional patent application in the United States. Patents in this family, if issued, will likely have a standard expiration date of August 9, 2040, subject to potential extensions.

We own one patent family directed to engineered meganucleases and methods of treatment targeting the transthyretin (TTR) gene, which is associated with TTR amyloidosis. This family includes two pending provisional patent applications in the United States. Patents in this family, if issued, will likely have a standard expiration date of March 26, 2040, subject to potential extensions.

We own one patent family directed to engineered meganucleases and methods of treatment targeting the dystrophin gene, which is associated with Duchenne Muscular Dystrophy. This family includes pending patent applications in the United States, Europe, Australia, Canada and Japan. Patents in this family, if issued, will have a standard expiration date of March 12, 2035, subject to potential extensions.

We own one patent family directed to engineered meganucleases and methods of treatment targeting genomic trinucleotide repeats, which are associated with several trinucleotide repeat disorders. This family includes pending patent applications in the United States and Europe. Patents in this family, if issued, will have a standard expiration date of May 2, 2036, subject to potential extensions.

We license from Duke one patent family directed to engineered fusion proteins comprising engineered meganuclease domains and effector domains which may be useful in controlling gene expression. This patent family includes a pending patent application in the United States. Patents in this family, if issued, will have a standard expiration date of October 18, 2026, subject to potential extensions.

We own one patent family directed to engineered meganucleases that target amplifiable genetic loci and may be useful in producing cells with amplified transgenes. This family includes one patent and one pending patent application in each of the United States and Europe. Patents in this family will have a standard expiration date of June 1, 2032, subject to potential extensions.

We own one patent family directed to self-limiting viral vectors (e.g., AAV vectors) that encode engineered meganucleases which eliminate the vector after gene delivery. This family includes pending patent applications in the United States and Europe. Patents in this family, if issued, will have a standard expiration date of June 20, 2036, subject to potential extensions.

We own one patent family directed to eukaryotic cells comprising a modified transferrin gene that includes an exogenous nucleic acid sequence encoding a polypeptide of interest. This family includes one pending provisional patent application in the United States. Patents in this family, if issued, will likely have a standard expiration date of January 11, 2040.

We own one patent family directed to methods for separation of empty and full AAV capsids during manufacturing. This family includes one pending provisional application in the United States. Patents in this family, if issued, will likely have a standard expiration date of February 7, 2040.

We own, through our Elo Life Systems subsidiary, an issued U.S. patent directed to engineered meganucleases which target a genetic locus in maize and methods for genetically modifying that locus in maize. That patent has a standard expiration date of March 2, 2029, subject to potential extensions.

For any individual patent, the term depends on the applicable law in the country in which the patent is granted. In most countries where we have filed patent applications or in-licensed patents and patent applications, patents have a term of 20 years from the application filing date or earliest claimed non-provisional priority date. In the United States, the patent term is 20 years but may be shortened if a patent is terminally disclaimed over another patent that expires earlier. The term of a U.S. patent may also be lengthened by a patent term adjustment to address administrative delays by the USPTO in granting a patent.

In the United States, the term of a patent that covers an FDA-approved drug or biologic may be eligible for patent term extension in order to restore the period of a patent term lost during the premarket FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the natural expiration of the patent. The patent term restoration period is generally equal to the portion of the FDA regulatory review period for the approved product that occurs after the date the patent issued, subject to certain exceptions. Only one patent may be extended for a regulatory review period for any product, and the application for the extension must be submitted prior to the expiration of the patent. In the future, we may decide to apply for restoration of patent term for one of our currently owned or licensed patents to extend its current expiration date, depending on the expected length of the clinical studies and other factors involved in the filing of the relevant BLA.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents or other intellectual property as an inventor or co-inventor. If we are required to and unable to obtain an exclusive license to any such third party co-owners' interest in such patent applications, such co-owners may be able to license their rights to other third parties, including our competitors. In addition, we may need the cooperation of any such co-owners to enforce any patents that issue from such patent applications against third parties, and such cooperation may not be provided to us. We or our licensors are subject to and may also become a party to similar proceedings or priority disputes in Europe or other foreign jurisdictions.

Our registered trademark portfolio currently contains three registered trademarks, specifically ARCUS, ARC nuclease, and Elo Life Systems, in the United States. In addition, our international portfolio contains seven registered trademarks around the world for ARCUS and ARC nuclease and includes one pending application in Australia for Elo Life Systems.

Licensed Intellectual Property

Duke University

In April 2006, we exclusively licensed from Duke families of patents and patent applications related to certain meganucleases and methods of making such nucleases owned by Duke. The patent family covered by the Duke License comprises the core patents covering ARCUS described above. See "—License and Collaboration Agreements—Duke University" above for additional information regarding the Duke License.

Cellectis S.A.

In January 2014, we entered into the Cellectis License, which relates to certain modified I-CreI homing endonuclease patents and patents that had been subject to litigation between us and Cellectis. The patents to which we have rights under the cross-license include at least eight issued patents in each of the United States and Australia, seven issued patents in Europe, two issued patents in Canada and one issued patent in Japan. These patents have standard expiration dates prior to January 29, 2034, subject to potential extensions. See "—License and Collaboration Agreements—Cellectis S.A." above for additional information regarding the Cellectis License.

Government Regulation

The FDA and other regulatory authorities at federal, state, and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring, and post-approval reporting of biological product candidates such as those we are developing. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Biologics Regulation

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

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's Good Laboratory Practice requirements, or GLPs;
- submission to the FDA of an Investigational New Drug application, or IND, which must become effective before clinical trials may begin;
- approval by an IRB or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA after completion of all pivotal clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

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

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

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some

studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

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

- Phase 1—The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.

- Phase 2—The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3—The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

- Phase 4—In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA.

Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Submission and Review by the FDA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by investigators. The submission of a BLA requires payment of a substantial user fee to FDA, and the sponsor of an approved BLA is also subject to an annual program fee. These fees are typically increased annually. A waiver of user fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Once a BLA has been submitted, the FDA's goal is to review standard applications within ten months after it accepts the application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. Priority review designation will direct overall attention and resources to the evaluation of applications for products that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions. Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

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

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a REMS to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase IV post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs. For example, in December 2016, the 21st Century Cures Act was signed into law. The Act is intended, among other things, to modernize the regulation of drugs and biologics and to spur innovation.

Expedited Development and Review Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. For a fast track product, the FDA may consider sections of the BLA for review on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable and the sponsor pays any required user fees upon submission of the first section of the application. A fast track designated product candidate may also qualify for priority review, under which the FDA sets the target date for FDA action on the BLA at six months after the FDA accepts the application for filing. Priority review is granted when there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious disease or condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of 10 months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the accelerated approval program, the FDA may approve a BLA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the biologic's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. FDA may withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product.

In addition, the Food and Drug Administration Safety and Innovation Act, or the FDASIA, which was enacted and signed into law in 2012, established the breakthrough therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If the FDA designates a breakthrough therapy, it may take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and considering alternative clinical trial designs when scientifically appropriate, which may result in smaller trials or more efficient trials that require less time to complete and may minimize the number of patients exposed to a potentially less efficacious treatment. Breakthrough therapy designation comes with all of the benefits of fast track designation, which means that the sponsor may file sections of the BLA for review on a rolling basis if certain conditions are satisfied, including an agreement with the FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review.

The Regenerative Medicine Advanced Therapy, or RMAT, designation facilitates an efficient development program for, and expedites review of, any drug that meets the following criteria: (1) it qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. Like breakthrough therapy designation, RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate, and eligibility for rolling review and priority review. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. RMAT-designated products that receive accelerated approval may, as appropriate, fulfill their post-approval requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence (such as electronic health records); through the collection of larger confirmatory data sets; or via post-approval monitoring of all patients treated with such therapy prior to approval of the therapy.

Fast track designation, priority review, breakthrough therapy designation and RMAT designation do not change the standards for approval but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

A designated orphan drug many not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if the second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. We plan to seek orphan drug designation for some or all of our product candidates in specific orphan indications in which there is a medically plausible basis for the use of these products.

Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Exclusivity

The Affordable Care Act, signed into law in 2010, includes a subtitle called the BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

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

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and impact of the BPCIA is subject to significant uncertainty.

Genetically Engineered Food Products

In the United States, the FDA and the USDA are primarily responsible for overseeing food regulation and safety, although many other federal agencies also play a role in food regulation.

USDA has jurisdiction over certain genetically engineered crops through the Animal and Plant Health Inspection Services, or APHIS. Under the Plant Protection Act and APHIS' Part 340 regulations, USDA requires anyone who wishes to import, transport interstate, or release into the environment a "regulated article" to apply for a permit or, in some cases, notify APHIS that the introduction will be made. Regulated articles are defined as "any organism which has been altered or produced through genetic engineering which USDA determines is a plant pest or has reason to believe is a plant pest." Regulated articles may be subject to extensive regulation, including both permitting requirements and inspections. However, to the extent products are subject to APHIS regulation, APHIS may make a determination of nonregulated status for a product following the submission of a petition requesting such a determination. The petition process can be a multi-year process that varies based on a number of factors, including APHIS's familiarity with similar products, the type and scope of the environmental review conducted, and the number and types of public comments received. APHIS conducts a comprehensive science-based review of the petition to assess, among other things, plant pest risk, environmental considerations pursuant to the National Environmental Policy Act of 1969, or NEPA, and any potential impact on endangered species. If, upon the completion of the review, APHIS grants the petition, the product is no longer deemed a "regulated article" and the petitioner may commercialize the product, subject to any conditions set forth in the decision. In January 2017, APHIS proposed significant amendments to its Part 340 regulatory framework that would, among other things, clarify the types of genetically engineered plants subject to regulation thereunder. In November 2017, however, APHIS withdrew its proposed rule and stated that it would "begin a fresh stakeholder engagement aimed at exploring alternative policy approaches." That process appears to remain ongoing.

On May 4, 2018, the USDA issued a proposed rule implementing the National Bioengineered Food Disclosure Standard, with a proposed compliance date of January 1, 2020. Under this proposed rule, the label of a bioengineered, or BE, food must include a disclosure that the food is a BE food or contains a BE ingredient, with certain exceptions. This proposed rule defines BE food as "a food that contains genetic material that was has been modified through in vitro recombinant deoxyribonucleic acid, or DNA, techniques and for which the modification could not otherwise be obtained through conventional breeding or found in nature," except in the case of an incidental additive present in food at an insignificant level and that does not have any technical or functional effect in the food. The USDA's proposed rule may change significantly prior to being finalized.

The FDA's oversight of food safety and security is primarily carried out by the Center for Food Safety and Applied Nutrition. To execute its responsibilities, the FDA conducts inspections and collects and analyzes product samples. Foods are typically not subject to premarket review and approval requirements, with limited exceptions, such as the requirement for premarket review and approval of food additives. Under Section 201(s) and 409 of the FDCA, any substance that is reasonably expected to become a component of food is considered a "food additive" that is subject to premarket approval by the FDA, unless it is already subject to a food additive regulation. Ingredients that are GRAS are exempt from the definition of food additive and from the premarket approval requirements. Under section 201(s), and FDA's implementing regulations, the use of a food substance may be GRAS either through a determination by qualified experts or, for a substance used in food before 1958, through experience based on common use in food.

Manufacturers of GRAS substances may voluntarily provide the FDA with a notification of GRAS determination, which includes, among other things, a description of the substance, the applicable conditions of use, the dietary exposure and an explanation of how the substance was determined to be safe for the intended use. Upon review of such a notification, the FDA may respond with a "no questions" letter stating that while it has not made its own GRAS determination, it has no questions at the time regarding the applicant's own GRAS determination. Alternatively, manufacturers may self-affirm that a given substance is GRAS without the voluntary FDA notification. A company may market a new food ingredient based on its independent determination that the substance is GRAS; however, the FDA can disagree with this determination and take enforcement action.

The FDA regulates foods made with genetically modified organisms under the approach summarized in its 1992 "Statement of Policy: Foods Derived from New Plant Varieties." Under this policy, updated in 2017, the FDA regulates foods derived from genetically modified plant varieties consistent with the framework for non-genetically modified foods. Under this framework, the FDA offers a voluntary consultation process to determine whether a food derived from a genetically modified plant variety raises any safety or other regulatory issues, such as whether any substance in the food from the plant may require premarket approval as a food additive.

Foreign Regulation

To market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union, or EU, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

To market a medicinal product in the European Economic Area, or EEA (which is comprised of the 28 Member States of the EU plus Norway, Iceland and Liechtenstein), we must obtain a Marketing Authorization, or MA. There are two types of marketing authorizations:

- The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced therapy products, and medicinal products containing a new active substance indicated for the treatment certain diseases, such as AIDS, cancer, neurodegenerative disorders, diabetes, auto immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the Centralized Procedure, the maximum timeframe for the evaluation of an MA application is 210 days, excluding clock stops. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Priority medicines scheme. The EMA has a so-called Priority Medicines, or PRIME, scheme. The PRIME scheme was launched in 2016 by the EMA to support the development and accelerate the review of new therapies to treat patients with unmet medical need. This voluntary scheme is based on enhanced interaction and early dialogue with developers of promising medicines, to optimize development plans and speed up evaluation so these medicines can reach patients earlier. To qualify for PRIME, product candidates require early clinical evidence that the therapy has the potential to offer a therapeutic advantage over existing treatments or benefits patients without treatment options. Among the benefits of PRIME are the appointment of a rapporteur to provide continuous support and help build knowledge ahead of an MA application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

Data and marketing exclusivity. In the EEA, new products authorized for marketing, or reference products, qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial authorization of the reference product in the EU. The 10 year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Pediatric investigation plan. In the EEA, marketing authorization applications for new medicinal products not authorized have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the marketing authorization is obtained in all Member States of the EU and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension.

Orphan drug designation. In the EEA, a medicinal product can be designated as an orphan drug if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or that the product is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Community and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

In the EEA, an application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, the EMA or the member state competent authorities, cannot accept another application for a marketing authorization, or grant a marketing authorization, for a similar medicinal product for the same indication. The period of market exclusivity is extended by two years for medicines that have also complied with an agreed PIP.

This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation, for example because the product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product, demonstration of "clinical superiority" by a similar medicinal product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply). Medicinal products designated as orphan drugs pursuant are eligible for incentives made available by the EU and its Member States to support research into, and the development and availability of, orphan drugs.

Clinical trials. Clinical trials of medicinal products in the European Union must be conducted in accordance with European Union and national regulations and the International Conference on Harmonization, or ICH, guidelines on GCPs. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of advanced therapy medicinal products. If the sponsor of the clinical trial is not established within the European Union, it must appoint an entity within the European Union to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

Prior to commencing a clinical trial, the sponsor must obtain a clinical trial authorization from the competent authority, and a positive opinion from an independent ethics committee. The application for a clinical trial authorization must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. Currently, clinical trial authorization applications must be submitted to the competent authority in each EU Member State in which the trial will be conducted. Under the new Regulation on Clinical Trials, which is currently expected to take effect in 2020, there will be a centralized application procedure where one national authority takes the lead in reviewing the application and the other national authorities have only a limited involvement. Any substantial changes to the trial protocol or other information submitted with the clinical trial applications must be notified to or approved by the relevant competent authorities and ethics committees. Medicines used in clinical trials must be manufactured in accordance with cGMP. Other national and European Union-wide regulatory requirements also apply.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our activities are potentially subject to regulation under various federal and state healthcare laws including, among others, the federal Anti-Kickback Statute, the federal False Claims Act and HIPAA.

The U.S. federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. A person does not need to have knowledge of the statute or specific intent to violate it to have committed a violation.

The U.S. federal civil and criminal false claims laws, including the civil False Claims Act, which can be enforced through civil whistleblower or qui tam actions, and civil monetary penalties laws, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. government. In addition, the government may assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

The U.S. Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers, as well as their business associates that perform certain services for or on their behalf involving the use or disclosure of individually identifiable health information.

Additionally, the federal Physician Payments Sunshine Act, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals beginning in 2022, and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually to CMS certain ownership and investment interests held by physicians and their immediate family members.

Moreover, analogous state and non-U.S. laws and regulations may apply to our activities, such as state anti-kickback and false claims laws, which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by the patients themselves, state laws that require pharmaceutical and device companies to comply with the industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources, state and local laws and regulations that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information, state and local laws which require the registration of pharmaceutical sales representatives and state and non-U.S. laws, such as the EU General Data Protection Regulation 2016/679, governing 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.

Efforts to ensure that current and future business arrangements with third parties complies with applicable healthcare laws and regulations involves substantial costs. If a business is found to be in violation of any of these or any other health regulatory laws that may apply to it, it may be subject to significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other U.S. healthcare programs, additional reporting requirements and oversight if subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of operations.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status for newly approved therapeutics. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Moreover, the coverage provided may be more limited than the purposes for which the product is approved by the FDA. It is also possible that a third-party payor may consider a product as substitutable and only offer to reimburse patients for the less expensive product. Adequate third-party payor reimbursement 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 payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell product candidates for which marketing approval is obtained. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively the Affordable Care Act, enacted in March 2010, has substantially changed healthcare financing and delivery by both governmental and private insurers. Among other things the Affordable Care Act included the following provisions:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to point-of-sale discounts of 70% off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the 340B Drug Discount Program;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; and
- a licensure framework for follow on biologic products.

On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or Texas District Court Judge, ruled that the entire Affordable Care Act is invalid based primarily on the fact that the legislation enacted on December 22, 2017, the Tax Cuts and Jobs Act of 2017, or the TCJA, repealed the tax-based shared responsibility payment imposed by the Affordable Care Act, on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate". On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the district court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how these decisions, subsequent appeals, if any, and other efforts to challenge, repeal or replace the Affordable Care Act will impact the Affordable Care Act.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute will remain in effect through 2029 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny recently over pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies, rebates and price negotiation for pharmaceutical products, some of which are included in the Trump administration's budget proposals for fiscal years 2019 and 2020, as well as recent bills introduced by the U.S. Senate and House of Representatives, respectively. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services has begun soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. Although a number of these, and other potential, proposed measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product and medical device pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and medical devices to purchase and which suppliers will be included in their prescription drug and other healthcare programs.

Additionally, 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 investigational new drug 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 products available to eligible patients as a result of the Right to Try Act.

Employees

As of December 31, 2019, we had 199 full-time Precisioneers, including 62 scientists with Ph.D. degrees. Of these full-time employees, 146 are engaged in research and development activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationships with our employees to be good.

Corporate Information

We were incorporated in Delaware in January 2006. Our principal executive offices are located at 302 East Pettigrew St., Suite A-100, Durham, North Carolina 27701, and our telephone number is (919) 314-5512. Our website address is www.precisionbiosciences.com. The information contained in, or accessible through, our website does not constitute a part of this Annual Report on Form 10-K.

Available Information

We file annual, quarterly and current reports, proxy statements and other information with the U.S. Securities and Exchange Commission ("SEC"). Our SEC filings are available to the public over the Internet at the SEC's website at *www.sec.gov*. Our SEC filings are also available free of charge under the Investors and Media section of our website at *www.precisionbiosciences.com* as soon as reasonably practicable after they are filed with or furnished to the SEC. Our website and the information contained on or connected to that site are not incorporated into this Annual Report on Form 10-K.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks described below, together with the other information included or incorporated by reference in this Annual Report on Form 10-K. The occurrence of any of the following risks could materially adversely affect our business, financial condition, results of operations and future growth prospects. In these circumstances, the market price of our common stock could decline.

Risks Related to Our Financial Condition, Limited Operating History and Need for Additional Capital

We have incurred significant operating losses since our inception and expect to continue to incur losses for the foreseeable future. We have never been profitable, and may never achieve or maintain profitability.

We have never been profitable and do not expect to be profitable in the foreseeable future. Since inception, we have incurred significant operating losses. If our product candidates are not successfully developed and approved, we may never generate any revenue from product sales. Our net losses were $92.9 million for the year ended December 31, 2019 and $46.0 million for the year ended December 31, 2018. As of December 31, 2019, we had an accumulated deficit of $177.1 million. In addition, we have not commercialized any products and have never generated any revenue from product sales. Substantially all of our losses have resulted from expenses incurred in connection with our research and development activities, including our preclinical development activities, and from general and administrative costs associated with our operations. We have financed our operations primarily through an initial public offering, or IPO, of our common stock, private placements of our convertible preferred stock and convertible debt and our development and commercial license agreement dated February 24, 2016, as amended, with Les Laboratoires Servier, which we refer to as the Servier Agreement. The amount of our future net losses will depend, in part, on the amount and growth rate of our expenses and our ability to generate revenues.

All of our current or future product candidates will require substantial additional development time and resources before we may realize revenue from product sales, if at all. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our current research and development programs, including conducting laboratory, preclinical and greenhouse studies for product candidates;
- continue to conduct or initiate clinical or field trials for product candidates;
- seek to identify, assess, acquire or develop additional research programs or product candidates;
- maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for any product candidates that may successfully complete development;
- establish a sales, marketing and distribution infrastructure to commercialize any products that may obtain marketing approval;
- further develop and refine the manufacturing process for our product candidates;
- change or add additional manufacturers or suppliers of biological materials or product candidates;
- validate our commercial-scale manufacturing facility, MCAT, as compliant with current Good Manufacturing Practices, or cGMP;
- further develop our genome editing technology;
- acquire or in-license other technologies;
- seek to attract and retain new and existing personnel;
- expand our facilities; and
- operate as a public company.

It will be several years, if ever, before we obtain regulatory approval for, and are ready for commercialization of, a therapeutic product candidate. Similarly, no product candidate from our food platform has advanced to field testing, and it will be several years, if ever, before we or our collaborators commercialize any such product candidate. New food and agriculture products using the precise editing approach generally take approximately three to five years to develop. Even if a therapeutic product candidate receives regulatory approval or a food or agriculture product advances through commercialization, future revenues for such product candidate will depend upon many factors, such as, as applicable, the size of any markets in which such product candidate is approved for sale, the market share captured by such product candidate, including as a result of the market acceptance of such product candidate and the effectiveness of manufacturing, sales, marketing and distribution operations related to such product candidate, the terms of any collaboration or other strategic arrangement we may have with respect to such product candidate and levels of reimbursement from third-party payors. If we are unable to develop and commercialize one or more product candidates either alone or with collaborators, or if revenues from any product candidate that receives marketing approval or is commercialized are insufficient, we may not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability. If we are unable to achieve and maintain profitability, the value of our common stock will be materially adversely affected.

We will need substantial additional funding, and if we are unable to raise a sufficient amount of capital when needed on acceptable terms, or at all, we may be forced to delay, reduce or eliminate some or all of our research programs, product development activities and commercialization efforts.

The process of identifying product candidates and conducting preclinical or greenhouse studies and clinical or field trials is time consuming, expensive, uncertain and takes years to complete. We expect our expenses to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate and continue clinical or field trials of, and seek marketing approval for, product candidates. In addition, if any therapeutic product candidate that we develop alone or with collaborators obtains marketing approval, we may incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution efforts. Furthermore, with the closing of our IPO, we expect to continue to incur additional 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 sufficient capital when needed, we may be forced to delay, reduce or eliminate current or future research programs, product development activities and/or commercialization efforts.

We expect that our existing cash and cash equivalents will be sufficient to fund our expected operating expenses and capital expenditure requirements into 2021. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our operating plans and other demands on our cash resources may change as a result of many factors, including factors unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations. We do not currently expect future grant revenues to be a material source of revenue. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop product candidates. Our future capital requirements will depend on many factors, including:

- the timing, scope, progress, costs, results and analysis of results of research activities, preclinical or greenhouse studies and clinical or field trials for any of our product candidates;
- the costs of future activities, including product manufacturing, sales, marketing and distribution activities for any product candidates that receive regulatory approval;
- the success of our existing collaborative relationships;
- the extent to which we exercise any development or commercialization rights under collaborative relationships;
- our ability to establish and maintain additional collaborative relationships on favorable terms, or at all;
- the extent to which we expand our operations and the timing of such expansion, including with respect to facilities, employees and product development platforms;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other technologies or product candidates;
- the extent to which we acquire or invest in other businesses;

- the costs of continuing to operate as a public company; and

- the amount of revenues, if any, received from commercial sales of any products that we develop alone or with collaborators that receive regulatory approval.

Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of specific strategic considerations. Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to obtain sufficient funding on a timely basis or on favorable terms, we may be required to significantly delay, reduce or eliminate one or more of our research or product development programs and/or commercialization efforts. We may also be unable to expand our operations or otherwise capitalize on business opportunities as desired. Any of these events could materially adversely affect our financial condition and business prospects.

Provisions of our debt instruments may restrict our ability to pursue our business strategies.

In May 2019, we entered into a loan and security agreement with Pacific Western Bank, or PWB, pursuant to which we may request advances on a revolving line of credit of up to an aggregate principal of $50.0 million, or the Revolving Line. The maturity date of the Revolving Line is May 15, 2022. As of December 31, 2019, we had no borrowings under our Revolving Line. Under the loan and security agreement, we granted PWB a security interest in substantially all of our assets, excluding any of the intellectual property now or hereafter owned, acquired or received by us (but including any rights to payment from the sale or licensing of any such intellectual property).

Our loan and security agreement with PWB requires us, and any debt instruments we may enter into in the future may require us, to comply with various covenants that limit our ability to, among other things:

- dispose of assets;

- change our name, location, executive office or executive management, business, fiscal year, or control;

- complete mergers or acquisitions;

- incur indebtedness;

- encumber assets;

- pay dividends or make other distributions to holders of our capital stock;

- make specified investments;

- make capitalized expenditures in excess of $40 million in the aggregate during each fiscal year; and

- engage in certain transactions with our affiliates.

These restrictions could inhibit our ability to pursue our business strategies. In addition, we are subject to financial covenants based on minimum cash balances.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity and/or debt financings and collaborations, licensing agreements or other strategic arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of such securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. To the extent that we raise additional capital through debt financing, it would result in increased fixed payment obligations and a portion of our operating cash flows, if any, being dedicated to the payment of principal and interest on such indebtedness. In addition, debt financing may involve agreements that include restrictive covenants that impose operating restrictions, such as restrictions on the incurrence of additional debt, the making of certain capital expenditures or the declaration of dividends. To the extent we raise additional capital through arrangements with collaborators or otherwise, we may be required to relinquish some of our technologies, research programs, product development activities, product candidates and/or future revenue streams, license our technologies and/or product candidates on unfavorable terms or otherwise agree to terms unfavorable to us. Furthermore, any capital raising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to advance research programs, product development activities or product candidates.

We have a limited operating history, which makes it difficult to evaluate our current business and future prospects and may increase the risk of your investment.

We are a genome editing company with a limited operating history. We formed our company in 2006 and spent the first nine years of our company's history developing and refining our core technology, and only during the past several years have we focused our efforts on advancing the development of product candidates.

Investment in biopharmaceutical and agricultural biotechnology product development is a highly speculative endeavor. It entails substantial upfront capital expenditures, and there is significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, obtain any required regulatory approvals or become commercially viable. Our genome editing platform and the technologies we are using are new and unproven. We have initiated a Phase 1/2a clinical trial in patients with relapsed or refractory, or R/R, non-Hodgkin lymphoma, or NHL, and R/R B-cell acute lymphoblastic leukemia, or B-ALL, but we have not commenced field trials for any of our product candidates from our food platform. We have not yet demonstrated an ability to successfully complete any clinical or field trials, obtain any required marketing approvals, manufacture products, conduct sales, marketing and distribution activities, or arrange for a third party to do any of the foregoing on our behalf. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing products.

Additionally, we encounter risks and difficulties frequently experienced by new and growing companies in rapidly developing and changing industries, including challenges in forecasting accuracy, determining appropriate investments of our limited resources, gaining market acceptance of our technology, managing a complex regulatory landscape and developing new product candidates, which may make it more difficult to evaluate our likelihood of success. Our current operating model may require changes in order for us to adjust to these challenges or scale our operations efficiently. Our limited operating history, particularly in light of the rapidly evolving nature of the biopharmaceutical and agricultural biotechnology industries and the genome editing field, may make it difficult to evaluate our technology and business prospects or to predict our future performance. Additionally, due to the stage of our operations, we expect that our financial condition and operating results may fluctuate significantly from quarter to quarter as a result of many factors as we build our business, and you should not rely upon the results of any particular quarterly or annual period as indications of future operating performance.

We may expend our limited resources on pursuing particular research programs or product candidates that may be less successful or profitable than other programs or product candidates.

Research programs to identify new product candidates and product development platforms require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs, product candidates or product development platforms that ultimately prove to be unsuccessful. Any time, effort and financial resources we expend on identifying and researching new product candidates and product development platforms may divert our attention from, and adversely affect our ability to continue, development and commercialization of existing research programs, product candidates and product development platforms. Clinical trials or field trials, as applicable, of any of our product candidates may never commence despite the expenditure of significant resources in pursuit of their development, and our spending on current and future research and development programs, product candidates and product development platforms may not yield any commercially viable products. As a result of having limited financial and managerial resources, we may forego or delay pursuit of opportunities 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. Additionally, 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 strategic arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We expect to take advantage of a Research and Development Tax Incentive program in Australia, which could be amended or changed.

We may be eligible to receive a financial incentive from the Australian government as part of its Research and Development Tax Incentive program, or R&D Tax Incentive program. The R&D Tax Incentive program is one of the key elements of the Australian government's support for Australia's innovation system and, if eligible, provides the recipient with a 43.5% refundable tax offset for research and development activities in Australia. There have been recent proposals to change the structure of the innovation and research and development funding landscape in Australia, which may impact the research and development tax incentive receivable for the 2019 financial year and beyond. There can be no assurance that we will qualify and be eligible for such incentives or that the Australian government will continue to provide incentives, offset, grants and rebates on similar terms or at all.

Risks Related to the Identification, Development and Commercialization of Our Product Candidates

ARCUS is a novel technology, making it difficult to predict the time, cost and potential success of product candidate development. We have not yet been able to assess the safety and efficacy of most of our product candidates in humans, and have only limited safety and efficacy information in humans to date regarding one of our product candidates.

Our success depends on our ability to develop and commercialize product candidates using our novel genome editing technology. The novel nature of our technology makes it difficult to accurately predict the developmental challenges we may face for product candidates as they proceed through research, preclinical or greenhouse studies and clinical or field trials. There have been a limited number of clinical trials of products created with genome editing technologies, only one of which has utilized our technology, and only two therapeutic products created with other genome editing technologies have received marketing approval in the United States. Because our therapeutic research programs are all in preclinical or early clinical stages, we have only been able to assess limited safety and efficacy data for one of our product candidates in a human trial. Current or future product candidates may not meet safety and efficacy requirements for continued development or ultimate approval in humans and may cause significant adverse events or toxicities. All of our product candidates are designed to act at the level of DNA, and because animal DNA differs from human DNA, it will be difficult for us to test our therapeutic product candidates in animal models for either safety or efficacy, and any testing that we conduct may not translate to their effects in humans. Moreover, animal models may not exist for some of the targets, diseases or indications that we intend to pursue. Similarly, we and our collaborators have not yet completed field trials for any agricultural product candidates created with our technology. Our product candidates may not be able to properly implement desired genetic edits with sufficient accuracy to be viable therapeutic or agricultural products, and there may be long-term effects associated with them that we cannot predict at this time. Any problems we experience related to the development of our genome editing technology or any of our or our collaborators' research programs or product candidates may cause significant delays or unanticipated costs, and we may not be able to satisfactorily solve such problems. These factors may prevent us or our collaborators from completing our preclinical or greenhouse studies or any clinical or field trials that we or our collaborators may initiate, or profitably commercializing any product candidates on a timely basis, or at all. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process as we develop and prepare to commercialize product candidates. These factors make it more difficult for us to predict the time, cost and potential success of product candidate development. If our product development activities take longer or cost more than anticipated, or if they ultimately are not successful, it would materially adversely affect our business and results of operations.

The genome editing field is relatively new and evolving rapidly, and other existing or future technologies may provide significant advantages over our ARCUS platform, which could materially harm our business.

To date, we have focused our efforts on optimizing our proprietary genome editing technology and exploring its potential applications. ARCUS is a novel genome editing technology using sequence-specific DNA-cutting enzymes, or nucleases, that is designed to perform modifications in the DNA of living cells and organisms. Other companies have previously undertaken research and development of genome editing technologies using zinc finger nucleases, transcription activator-like effector nucleases, or TALENs, and clustered regularly interspaced short palindromic repeats associated protein-9 nuclease, or CRISPR/Cas9, although none has obtained marketing approval for a product candidate developed using such technologies. Other genome editing technologies in development or commercially available, or other existing or future technologies, may lead to treatments or products that may be considered better suited for use in human therapeutics or agriculture, which could reduce or eliminate our commercial opportunity.

We are heavily dependent on the successful development and translation of ARCUS, and due to the early stages of our product development operations, we cannot give any assurance that any product candidates will be successfully developed and commercialized.

We are at an early stage of development of the product candidates currently in our programs and are continuing to develop our ARCUS technology. To date, we have invested substantially all of our efforts and financial resources to develop ARCUS and advance our current product development programs, including conducting preclinical studies, early stage clinical trials and other early research and development activities, and providing general and administrative support for these operations. Our future success is dependent on our ability to successfully develop and, where applicable, obtain regulatory approval for, including marketing approval for, and then successfully commercialize, product candidates, either alone or with collaborators. We have not yet developed and commercialized any product candidates, and we may not be able to do so, alone or with collaborators.

Our research and development programs may not lead to the successful identification, development or commercialization of any products.

The success of our business depends primarily upon our ability to identify, develop and commercialize products using our genome editing technology. With the exception of our CD19 product candidate, all current product candidates and product development programs are still in the discovery, preclinical or greenhouse stages. We may be unsuccessful in advancing those product candidates into clinical development or field trials or in identifying any developing additional product candidates. Our ability to identify and develop product candidates is subject to the numerous risks associated with preclinical and early stage biotechnology development activities, including that:

- the use of ARCUS may be ineffective in identifying additional product candidates;
- we may not be able to assemble sufficient resources to acquire or discover additional product candidates;
- we may not be able to enter into collaborative arrangements to facilitate development of product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- our product candidates may be covered by third parties' patents or other exclusive rights;
- the regulatory pathway for a product candidate may be too complex, expensive or otherwise difficult to navigate successfully; or
- our product candidates may be shown to not be effective, have harmful side effects or otherwise pose risks not outweighed by such product candidate's benefits or have other characteristics that may make the products impractical to manufacture, unlikely to receive any required marketing approval, unlikely to generate sufficient market demand or otherwise not achieve profitable commercialization.

Our product candidates currently being investigated in clinical trials, or that are expected to be investigated in clinical trials, and other product candidates we may identify may never be approved. Failure to successfully identify and develop new product candidates and obtain regulatory approvals for our products would have a material adverse effect on our business and financial condition and could cause us to cease operations.

If our product candidates do not achieve projected development milestones or commercialization in the announced or expected timeframes, the further development or commercialization of such product candidates may be delayed, and our business will be harmed.

We sometimes estimate, or may in the future estimate, the timing of the accomplishment of various scientific, clinical, manufacturing, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies or clinical or field trials, the submission of regulatory filings, the receipt of marketing approval or the realization of other commercialization objectives. The achievement of many of these milestones may be outside of our control. All of these milestones are based on a variety of assumptions, including assumptions regarding capital resources, constraints and priorities, progress of and results from development activities and the receipt of key regulatory approvals or actions, any of which may cause the timing of achievement of the milestones to vary considerably from our estimates. If we or our collaborators fail to achieve announced milestones in the expected timeframes, the commercialization of the product candidates may be delayed, our credibility may be undermined, our business and results of operations may be harmed, and the trading price of our common stock may decline.

Adverse public perception of genome editing may negatively impact the developmental progress or commercial success of products that we develop alone or with collaborators.

The developmental and commercial success of our current product candidates, or any that we develop alone or with collaborators in the future, will depend in part on public acceptance of the use of genome editing technology for the prevention or treatment of human diseases or for application in food or agricultural products. Adverse public perception of applying genome editing technology for these purposes may negatively impact our ability to raise capital or enter into strategic agreements for the development of product candidates.

The commercial success of any food or agricultural products that we develop alone or with collaborators may be adversely affected by claims that biotechnology plant products are unsafe for consumption or use, pose risks of damage to the environment or create legal, social or ethical dilemmas. Additionally, the public may perceive any potential food or agricultural products created with ARCUS to constitute genetically modified organisms, or GMO, even if they do not constitute genetically modified organisms under relevant regulatory requirements, and may be unwilling to consume them because of negative opinions regarding consumption of genetically modified organisms. This may result in expenses, delays or other impediments to development programs in our food platform or the market acceptance and commercialization of any potential food or agricultural products.

Any therapeutic product candidates may involve editing the human genome. The commercial success of any such potential therapeutic products, if successfully developed and approved, may be adversely affected by claims that genome editing is unsafe, unethical or immoral. This may lead to unfavorable public perception and the inability of any therapeutic product candidates to gain the acceptance of the public or the medical community. Unfavorable public perceptions may also adversely impact our or our collaborators' ability to enroll clinical trials for therapeutic product candidates. Moreover, success in commercializing any therapeutic product candidates that receive regulatory approval will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of such product candidates in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available. Publicity of any adverse events in, or unfavorable results of, preclinical studies or clinical trials for any current or future product candidates, or with respect to the studies or trials of our competitors or of academic researchers utilizing genome editing technologies, even if not ultimately attributable to our technology or product candidates, could negatively influence public opinion. Negative public perception about the use of genome editing technology in human therapeutics and food or agricultural products, whether related to our technology or a competitor's technology, could result in increased governmental regulation, delays in the development and commercialization of product candidates or decreased demand for the resulting products, any of which may have a negative impact on our business and financial condition.

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

The development and commercialization of new drug products is highly competitive, and the genome editing field is characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We will face competition with respect to our current and future therapeutic product candidates from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization of products. Competition for improving plant genetics comes from conventional and advanced plant breeding techniques, as well as from the development of advanced biotechnology traits. Other potentially competitive sources of improvement in crop yields include improvements in crop protection chemicals, fertilizer formulations, farm mechanization, other biotechnology and information management. Programs to improve genetics and crop protection chemicals are generally concentrated within a relatively small number of large companies, while non-genetic approaches are underway with a broader set of companies.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs. Some of these competitive products and therapies are based on scientific approaches that are similar to our approach, and others are based on entirely different approaches. We principally compete with others developing and utilizing genome editing technology in the human health and plant sciences sectors, including companies such as Cellectis S.A., CRISPR Therapeutics, AG, Editas Medicine, Inc., Intellia Therapeutics, Inc. and Sangamo Therapeutics, Inc. Several companies, including Novartis Pharmaceuticals Corp. and Gilead Sciences, Inc., or Gilead, have obtained FDA approval for autologous immunotherapies, and a number of companies, including Cellectis S.A., Celgene Corp., Allogene Therapeutics and CRISPR Therapeutics AG, are pursuing allogeneic immunotherapies. We expect that our operations focused on developing products for *in vivo* gene correction will face substantial competition from others focusing on gene therapy treatments, especially those that may focus on conditions that our product candidates target. Moreover, any human therapeutics products that we develop alone or with collaborators will compete with existing standards of care for the diseases and conditions that our product candidates target and other types of treatments, such as small molecule, antibody or protein therapies. Our competitors in the agricultural biotechnology space include Pairwise Plants, LLC, Caribou Biosciences, Inc., Corteva Agriscience, Tropic Biosciences UK LTD, Calyxt, Inc., Benson Hill Biosystems and Cibus.

Many of our current or potential competitors, either alone or with their collaborators, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical or greenhouse testing, conducting clinical or field trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and agricultural biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products we develop alone or with collaborators or that would render any such products obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we or our collaborators may obtain approval for any that we develop, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our product candidates uneconomical or obsolete, and we or our collaborators may not be successful in marketing any product candidates we may develop against competitors. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we develop alone or with collaborators.

Our future profitability, if any, depends in part on our and our collaborators' ability to penetrate global markets, where we would be subject to additional regulatory burdens and other risks and uncertainties associated with international operations that could materially adversely affect our business.

Our future profitability, if any, will depend in part on our ability and the ability of our collaborators to commercialize any products that we or our collaborators may develop in markets throughout the world. Commercialization of products in various markets could subject us to risks and uncertainties, including:

- obtaining, on a country-by-country basis, the applicable marketing authorization from the competent regulatory authority;
- the burden of complying with complex and changing regulatory, tax, accounting, labor and other legal requirements in each jurisdiction that we or our collaborators pursue;
- reduced protection for intellectual property rights;
- differing medical and agricultural practices and customs affecting acceptance in the marketplace;
- import or export licensing requirements;
- governmental controls, trade restrictions or changes in tariffs;
- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers;
- foreign currency exchange rate fluctuations;
- foreign reimbursement, pricing and insurance regimes; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

We have no prior experience in these areas, and our collaborators may have limited experience in these areas. Failure to successfully navigate these risks and uncertainties may limit or prevent market penetration for any products that we or our collaborators may develop, which would limit their commercial potential and our revenues.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any products that we develop alone or with collaborators.

We face an inherent risk of product liability and professional indemnity exposure related to the testing in clinical or field trials of our product candidates. We will face an even greater liability risk if we commercially sell any products that we or our collaborators may develop for human use or consumption. Manufacturing defects, errors in product distribution or storage processes, improper administration or application and known or unknown side effects of product usage may result in liability claims against us or third parties with which we have relationships. These actions could include claims resulting from acts by our collaborators, licensees and subcontractors over which we have little or no control.

For example, our liability could be sought by patients participating in clinical trials for potential therapeutic product candidates as a result of unexpected side effects, improper product administration or the deterioration of a patient's condition, patient injury or even death. Criminal or civil proceedings might be filed against us by patients, regulatory authorities, biopharmaceutical companies and any other third party using or marketing any product candidates or products that we develop alone or with collaborators. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated adverse effects. If we cannot successfully defend ourselves against claims that product candidates or products we develop alone or with collaborators caused harm, we could incur substantial liabilities.

Regardless of merit or eventual outcome, liability claims may result in:

- significant time and costs to defend the related litigation;
- injury to our reputation and significant negative media attention;
- diversion of management's attention from pursuing our strategy;
- withdrawal of clinical trial participants;
- delay or termination of clinical trials;
- decreased demand for any products that we develop alone or with collaborators;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to further develop or commercialize any products.

Although the clinical trial process is designed to identify and assess potential side effects, clinical development does not always fully characterize the safety and efficacy profile of a new medicine, and it is always possible that a drug or biologic, even after regulatory approval, may exhibit unforeseen side effects. If our product candidates were to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. If any of our product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us and the safety and quality of such products. We could be adversely affected if we are subject to negative publicity associated with illness or other adverse effects resulting from patients' use or misuse of such products or any similar products distributed by other companies.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage if we or our collaborators successfully commercialize any products. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liabilities to which we may become subject.

Additional Risks Related to the Identification, Development and Commercialization of Our Therapeutic Product Candidates

The regulatory landscape that will apply to development of therapeutic product candidates by us or our collaborators is rigorous, complex, uncertain and subject to change, which could result in delays or termination of development of such product candidates or unexpected costs in obtaining regulatory approvals.

Regulatory requirements governing products created with genome editing technology or involving gene therapy treatment have changed frequently and will likely continue to change in the future. Approvals by one regulatory agency may not be indicative of what any other regulatory agency may require for approval, and there has historically been substantial, and sometimes uncoordinated, overlap in those responsible for regulation of gene therapy products, cell therapy products and other products created with genome editing technology. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Our product candidates will need to meet safety and efficacy standards applicable to any new biologic under the regulatory framework administered by the FDA.

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 subject to the NIH Guidelines are subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. We are subject to significant regulatory oversight by the FDA, and in addition to the government regulators, the applicable IBC and institutional review board, or IRB, of each institution at which we or our collaborators conduct clinical trials of our product candidates, or a central IRB if appropriate, would need to review and approve the proposed clinical trial.

The same applies in the European Union, or the EU. The European Medicines Agency, or the EMA, has a Committee for Advanced Therapies, or CAT, that is responsible for assessing the quality, safety and efficacy of advanced-therapy medicinal products. Advanced-therapy medical products include gene therapy medicine, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. In the EU, the development and evaluation of a gene therapy medicinal product must be considered in the context of the relevant EU guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines. Similarly complex regulatory environments exist in other jurisdictions in which we might consider seeking regulatory approvals for our product candidates, further complicating the regulatory landscape. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any of our gene therapy or genome editing product candidates, but that remains uncertain at this point.

The clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to evaluate the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for product candidates created with novel genome editing technology such as ours can be more lengthy, rigorous and expensive than the process for other better known or more extensively studied product candidates and technologies. Since we are developing novel treatments for diseases in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the EMA or comparable regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. This may be a particularly significant risk for many of the genetically defined diseases for which we may develop product candidates alone or with collaborators due to small patient populations for those diseases, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing genome editing technology in a timely manner or under technically or commercially feasible conditions. Even if our product candidates obtain required regulatory approvals, such approvals may later be withdrawn as a result of changes in regulations or the interpretation of regulations by applicable regulatory agencies.

Changes in applicable regulatory guidelines may lengthen the regulatory review process for our product candidates, require additional studies or trials, increase development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of such product candidates, or lead to significant post-approval limitations or restrictions. Additionally, adverse developments in clinical trials conducted by others of gene therapy products or products created using genome editing technology, such as products developed through the application of a CRISPR/Cas9 technology, or adverse public perception of the field of genome editing, may cause the FDA, the EMA and other regulatory bodies to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing genome editing technologies, either of which could materially harm our business. Furthermore, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the development or commercialization of current or future product candidates.

As we advance product candidates alone or with collaborators, we will be required to consult with these regulatory and advisory groups and comply with all applicable guidelines, rules and regulations. If we fail to do so, we or our collaborators may be required to delay or terminate development of such product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a product candidate to market could decrease our ability to generate sufficient product revenue to maintain our business.

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

We plan to submit IND applications to enable us to conduct clinical trials for additional product candidates in the future, and we expect to file IND amendments to enable us to conduct additional clinical trials under existing INDs. We cannot be sure that submission of an IND application or IND amendment will result in us being allowed to proceed with clinical trials, or that, once begun, issues will not arise that could result in the suspension or termination such clinical trials. The manufacturing of allogeneic CAR T cell therapy remains an emerging and evolving field. Accordingly, we expect chemistry, manufacturing and controls-related topics, including product specifications, will be a focus of IND reviews, which may delay receipt of authorization to proceed under INDs. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND or clinical trial application, we cannot guarantee that such regulatory authorities will not change their requirements in the future.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

We and any collaborators are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the EMA, impose similar requirements. The time required to obtain approval by the FDA, the EMA and comparable foreign authorities is unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including substantial discretion of the regulatory authorities and sufficient resources at the FDA. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. To date, we have not submitted a biologics license application, or BLA, or other marketing authorization application to the FDA or similar drug approval submissions to comparable foreign regulatory authorities for any product candidate. We and any collaborators must complete additional preclinical or nonclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates in humans to the satisfaction of the regulatory authorities before we will be able to obtain these approvals.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our or our collaborators' clinical trials;
- we or our collaborators may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we or our collaborators may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our or our collaborators' interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of product candidates may not be sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we or our collaborators contract for clinical and commercial supplies;
- the FDA or comparable foreign regulatory authorities may fail to approve the companion diagnostics we contemplate developing with collaborators; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our or our collaborators' clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, or a Risk Evaluation and Mitigation Strategy, or REMS. Regulatory authorities may not approve the price we or our collaborators intend to charge for products we may develop, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Clinical trials are difficult to design and implement, expensive, time-consuming and involve an uncertain outcome, and the inability to successfully and timely conduct clinical trials and obtain regulatory approval for our product candidates would substantially harm our business.

Clinical testing is expensive and usually takes many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process, and product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. We have initiated a Phase 1/2a clinical trial in patients with R/R NHL or R/R B-ALL, and expect to initiate an additional Phase 1/2a clinical trial in subjects with NHL, chronic lymphocytic leukemia and small lymphocytic lymphoma in the first quarter of 2020. We do not know whether any current or planned clinical trials will need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Clinical trials can be delayed, suspended or terminated for a variety of reasons, including in connection with:

- the inability to generate sufficient preclinical, toxicology or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- applicable regulatory authorities disagreeing as to the design or implementation of the clinical trials;
- obtaining regulatory authorization to commence a trial;
- reaching an agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining IRB approval at each site;
- developing and validating the companion diagnostic to be used in a clinical trial, if applicable;
- insufficient or inadequate supply or quality of product candidates or other materials, including identification of lymphocyte donors meeting regulatory standards necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- recruiting and retaining enough suitable patients to participate in a trial;
- having enough patients complete a trial or return for post-treatment follow-up;
- adding a sufficient number of clinical trial sites;
- inspections of clinical trial sites or operations by applicable regulatory authorities, or the imposition of a clinical hold;
- clinical sites deviating from trial protocol or dropping out of a trial;
- the inability to demonstrate the efficacy and benefits of a product candidate;
- discovering that product candidates have unforeseen safety issues, undesirable side effects or other unexpected characteristics;
- addressing patient safety concerns that arise during the course of a trial;
- receiving untimely or unfavorable feedback from applicable regulatory authorities regarding the trial or requests from regulatory authorities to modify the design of a trial;
- non-compliance with applicable regulatory requirements by us or third parties or changes in such regulations or administrative actions;
- suspensions or terminations by IRBs of the institutions at which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities due to a number of factors, including those described above;
- third parties being unable or unwilling to satisfy their contractual obligations to us; or
- changes in our financial priorities, greater than anticipated costs of completing a trial or our inability to continue funding the trial.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Additionally, we or our collaborators may experience unforeseen events during or resulting from clinical trials that could delay or prevent receipt of marketing approval for or commercialization of product candidates. For example, clinical trials of product candidates may produce negative, inconsistent or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs. Regulators may also revise the requirements for approving the product candidates, or such requirements may not be as we anticipate. If we or our collaborators are required to conduct additional clinical trials or other testing of product candidates beyond those that we or our collaborators currently contemplate, if we or our collaborators are unable to successfully complete clinical trials or other testing of such product candidates, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining or fail to obtain marketing approval for product candidates;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements;
- be subject to changes in the way the product is administered;
- have regulatory authorities withdraw or suspend their approval of the product or impose restrictions on its distribution;
- be sued; or
- experience damage to our reputation.

If we or our collaborators experience delays in the commencement or completion of our clinical trials, or if we or our collaborators terminate a clinical trial prior to completion, we may experience increased costs, have difficulty raising capital and/or be required to slow down the development and approval process timelines. Furthermore, the product candidates that are the subject of such trials may never receive regulatory approval, and their commercial prospects and our ability to generate product revenues from them could be impaired or not realized at all.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authorities may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authorities, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Any product candidates that we or our collaborators may develop will be novel and may be complex and difficult to manufacture, and if we experience manufacturing problems, it could result in delays in development and commercialization of such product candidates or otherwise harm our business.

Our product candidates involve or will involve novel genome editing technology and will require processing steps that are more complex than those required for most small molecule drugs, resulting in a relatively higher manufacturing cost. Moreover, unlike small molecules, the physical and chemical properties of biologics generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that such product will perform in the intended manner. Although we intend to employ multiple steps to control the manufacturing process, we may experience manufacturing issues with any of our product candidates that could cause production interruptions, including contamination, equipment or reagent failure, improper installation or operation of equipment, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error, disruptions in the operations of our suppliers, inconsistency in cell growth and variability in product characteristics. We may

encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other comparable applicable standards or specifications with consistent and acceptable production yields and costs. For example, the FDA has required us to conduct testing of our allogeneic CAR T cell product candidates for the presence of certain human viruses prior to release of such products for clinical use. If the FDA concludes that further such viral testing of our product candidates is required and that any lots testing positive may not be used in clinical trials, we may need to produce new clinical trial materials, which could delay our clinical trials and result in higher manufacturing costs. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our product candidates or in the manufacturing facilities in which such product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. Our manufacturing process for any allogeneic CAR T cell product candidate that we develop alone or with collaborators will be susceptible to product loss or failure due to the quality of the raw materials, failure of the products to meet specifications, logistical issues associated with the collection of white blood cells, or starting material, from healthy third-party donors, shipping such material to the manufacturing site, ensuring standardized production batch-to-batch in the context of mass production, freezing the manufactured product, shipping the final product globally and infusing patients with such product. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, delays in initiating or completing clinical trials, product recalls, product liability claims or insufficient inventory.

As product candidates are developed through preclinical to late-stage clinical trials towards approval and commercialization, we expect that various aspects of the development program, such as manufacturing methods, may be altered along the way in an effort to help optimize processes and results. Such changes carry the risk that they will not achieve the intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of future clinical trials or our reliance on results of trials that have previously been conducted using the product candidate in its previous form. If the manufacturing process is changed during the course of product development, we or our collaborators may be required to repeat some or all of the previously conducted trials or conduct additional bridging trials, which could increase our costs and delay or impede our ability to obtain marketing approval.

We expect our manufacturing strategy for one or more of our product candidates may involve the use of contract manufacturing organizations, or CMOs, as well as our newly opened manufacturing facility, the MCAT. The facilities used by us and our contract manufacturers to manufacture therapeutic product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our BLA to the FDA. We do not control the manufacturing process of, and are currently completely dependent on, our contract manufacturing partners for compliance with cGMP, for the manufacture of our product candidates. We may establish multiple manufacturing facilities as we expand our commercial footprint to multiple geographies, which will be costly and time consuming and may lead to regulatory delays. Even if we are successful, our manufacturing capabilities could be affected by cost-overruns, potential problems with scale-out, process reproducibility, stability issues, lot inconsistency, timely availability of reagents or raw materials, unexpected delays, equipment failures, labor shortages, natural disasters, utility failures, regulatory issues and other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

The FDA, the EMA and other foreign regulatory authorities may require us to submit samples of any lot of any product that may receive approval together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other foreign regulatory authorities may require that we not distribute a lot until the relevant agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us or our collaborators to delay product launches or clinical trials, which could be costly to us and otherwise harm our business. Problems in our manufacturing process also could restrict our or our collaborators' ability to meet market demand for products.

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

We will rely on donors of T cells to manufacture product candidates from our allogeneic CAR T immunotherapy platform, and if we do not obtain an adequate supply of T cells from qualified donors, development of those product candidates may be adversely impacted.

We are developing a pipeline of allogeneic T cell product candidates that are engineered from healthy donor T cells, which vary in type and quality. This variability in type and quality of a donor's T cells makes producing standardized product candidates more difficult and makes the development and commercialization pathway of those product candidates more uncertain. We 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. If we are unable to identify and obtain T cells from donors that satisfy our criteria in sufficient quantity, to obtain such cells in a timely manner or to address variability in donor T cells, development of our CAR T cell product candidates may be delayed or there may be inconsistencies in the product candidates we produce, which could negatively impact development of such product candidates, harm our reputation and adversely impact our business and prospects.

Failure to achieve operating efficiencies from MCAT may require us to devote additional resources and management time to manufacturing operations and may delay our product development timelines.

We have leased approximately 33,600 square feet of space for MCAT at a location approximately seven miles from our headquarters in Durham, North Carolina. We intend to begin using this new manufacturing center to create clinical trial material for certain of our planned clinical trials in 2020. We may not experience the anticipated operating efficiencies as we commence manufacturing. Any delays in manufacturing may disrupt or delay the supply of our product candidates if we have not maintained a sufficient back-up supply of such product candidates through third-party manufacturers. Moreover, changing manufacturing facilities may also require that we or our collaborators conduct additional studies, make notifications to regulatory authorities, make additional filings to regulatory authorities, and obtain regulatory authority approval for the new facilities, which may be delayed or which we may never receive. We will further need to comply with the FDA's and applicable foreign regulatory authorities' cGMP requirements for the production of product candidates for clinical trials and, if approved, commercial supply, and will be subject to FDA and comparable foreign regulatory authority inspection. These requirements include the qualification and validation of our manufacturing equipment and processes. We may not be able to develop or acquire the internal expertise and resources necessary for compliance with these requirements. Should we fail to comply with cGMP requirements, the opening of our manufacturing facility will be delayed. If we fail to achieve the operating efficiencies that we anticipate, our manufacturing and operating costs may be greater than expected, which could have a material adverse impact on our operating results.

We also may encounter problems hiring and retaining the experienced scientific, quality-control and manufacturing personnel needed to operate our manufacturing processes. If we experience unanticipated employee shortage or turnover in any of these areas, we may not be able to effectively manage our ongoing manufacturing operations and we may not achieve the operating efficiencies that we anticipate from the new facility, which may negatively affect our product development timeline or result in difficulties in maintaining compliance with applicable regulatory requirements.

Any such problems could result in the delay, prevention or impairment of clinical development and commercialization of our product candidates.

We or our collaborators may experience delays or difficulties in enrolling patients in clinical trials, which could delay or prevent receipt of regulatory approvals.

We or our collaborators may not be able to initiate or continue clinical trials on a timely basis or at all for any product candidates we or our collaborators identify or develop if we or our collaborators are unable to locate and enroll a sufficient number of eligible patients to participate in the trials as required by applicable regulations or as needed to provide appropriate statistical power for a given trial. Additionally, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as one or more of our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in our competitors' clinical trials.

Patient enrollment may also be affected by many factors, including:

- severity and difficulty of diagnosing of the disease under investigation;
- size of the patient population and process for identifying subjects;
- eligibility and exclusion criteria for the trial in question;
- our or our collaborators' ability to recruit clinical trial investigators with the appropriate competencies and experience;
- design of the trial protocol;
- availability and efficacy of approved medications or therapies, or other clinical trials, for the disease or condition under investigation;
- perceived risks and benefits of the product candidate under trial or testing, or of the application of genome editing to human indications;
- availability of genetic testing for potential patients;
- efforts to facilitate timely enrollment in clinical trials;

- patient referral practices of physicians;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

We expect that some of our product candidates will focus on rare genetically defined diseases with limited patient pools from which to draw for enrollment in clinical trials. The eligibility criteria of our clinical trials will further limit the pool of available trial participants. In addition to the factors identified above, patient enrollment in any clinical trials we or our collaborators may conduct may be adversely impacted by any negative outcomes our competitors may experience, including adverse side effects, clinical data showing inadequate efficacy or failures to obtain regulatory approval.

Furthermore, our or our collaborators' ability to successfully initiate, enroll and conduct a clinical trial outside the United States is subject to numerous additional risks, including:

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

Enrollment delays in clinical trials may result in increased development costs for any of our product candidates, which may cause the value of our company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which may have an adverse effect on our results of operations and prospects.

Results of preclinical studies and early clinical trials of product candidates may not be predictive of results of later studies or trials. Our product candidates may not have favorable results in later clinical trials, if any, or receive regulatory approval.

Preclinical and clinical drug development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the preclinical study or clinical trial process. Despite promising preclinical or clinical results, any product candidate can unexpectedly fail at any stage of preclinical or clinical development. The historical failure rate for product candidates in our industry is high.

The results from preclinical studies or early clinical trials of a product candidate may not be predictive of the results from later preclinical studies or clinical trials, and interim results of a clinical trial are not necessarily indicative of final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through preclinical studies and initial clinical trials. Many companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks at later stages of development after achieving positive results in early stages of development, and we may face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including previously unreported adverse events. Moreover, non-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain regulatory approval. With the exception of our allogeneic anti-CD19 CAR T product candidate, which has undergone limited testing in humans to date, our gene editing technology and our product candidates have never undergone testing in humans and have only been tested in a limited manner in animals, and results from animal studies may not be predictive of clinical trial results. Even if product candidates progress to clinical trials, these product candidates may fail to show the safety and efficacy in clinical development required to obtain regulatory approval, despite the observation of positive results in animal studies. Our or our collaborators' failure to replicate positive results from early research programs and preclinical or greenhouse studies may prevent us from further developing and commercializing those or other product candidates, which would limit our potential to generate revenues from them and harm our business and prospects.

For the foregoing reasons, we cannot be certain that any ongoing or future preclinical studies or clinical trials will be successful. Any safety or efficacy concerns observed in any one of our preclinical studies or clinical trials in a targeted area could limit the prospects for regulatory approval of product candidates in that and other areas, which could have a material adverse effect on our business and prospects.

Interim "top-line" and initial data from studies or trials that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim "top-line" or initial data from preclinical or greenhouse studies or clinical or field trials. For example, we recently reported initial results from our ongoing Phase 1/2a clinical trial of PBCAR0191. Interim data are subject to the risk that one or more of the outcomes may materially change as more 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 and carefully evaluate all data. As a result, the top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Initial or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from these initial data we previously published. As a result, interim and initial data should be viewed with caution until the final data are available. Additionally, interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between initial or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the top-line data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, product candidates may be harmed, which could significantly harm our business prospects.

If any of our product candidates do not work as intended or cause undesirable side effects, it could hinder or prevent receipt of regulatory approval or realization of commercial potential for them or our other product candidates and could substantially harm our business.

Our product candidates may be associated with off-target editing or other serious adverse events, undesirable side effects or unexpected characteristics. Results of clinical trials could reveal severe or recurring side effects, toxicities or unexpected events, including death. Off-target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA. In those instances where we also provide a segment of DNA, it is possible that following off-target cut events, such DNA could be integrated into the genome at an unintended site, potentially disrupting another important gene or genomic element. There may also be delayed adverse events following exposure to therapeutics made with genome editing technologies due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. In addition to serious adverse events or side effects caused by product candidates we develop alone or with collaborators, the administration process or related procedures may also cause undesirable side effects. Any side effects may not be appropriately recognized or managed by the treating medical staff. We or our collaborators expect to have to educate medical personnel using any product candidates we may develop to understand the side effect profiles for our clinical trials and upon any commercialization of such product candidates. Inadequate recognition or management of the potential side effects of such product candidates could result in patient injury or death.

If any such events occur, clinical trials or commercial distribution of any product candidates or products we develop alone or with collaborators could be suspended or terminated, and our business and reputation could suffer substantial harm. Treatment-related side effects could affect patient recruitment and the ability of enrolled patients to complete the trial or result in potential liability claims. Regulatory authorities could order us or our collaborators to cease further development of, deny approval of or require us to cease selling any product candidates or products for any or all targeted indications. If we or our collaborators elect, or are required, to delay, suspend or terminate any clinical trial or commercialization efforts, the commercial prospects of such product candidates or products may be harmed, and our ability to generate product revenues from them or other product candidates that we develop may be delayed or eliminated.

Additionally, if we successfully develop a product candidate alone or with collaborators and it receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of treatment with such product candidate outweigh the risks for each potential patient, which may include, among other things, a communication plan to health care practitioners, patient education, extensive patient monitoring or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry. We or our collaborators may also be required to adopt a REMS or engage in similar actions, such as patient education, certification of health care professionals or specific monitoring, if we or others later identify undesirable side effects caused by any product that we develop alone or with collaborators. Such identification could also have several additional significant negative consequences, such as:

- regulatory authorities may suspend, withdraw or limit approvals of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings on the label, including "boxed" warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way a product is administered or conduct additional trials;
- the product may become less competitive;
- we or our collaborators may decide to remove the product from the marketplace;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- we could be sued and be held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us or our collaborators from achieving or maintaining market acceptance of any potential product.

We are subject to federal, state and non-U.S. healthcare and data privacy and security laws and regulations relating to our business, and could face substantial penalties if we are determined not to have fully complied with such laws, which would have an adverse impact on our business.

Our business operations, as well as our current and anticipated future arrangements with investigators, healthcare professionals, consultants, third-party payors, customers and patients, expose or will expose us to broadly applicable foreign, federal, and state fraud and abuse and other healthcare and privacy laws and regulations. These laws constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute any potential products for which we may obtain marketing approval. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a U.S. healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the U.S. federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation;
- U.S. federal civil and criminal false claims laws, including the civil False Claims Act, which can be enforced through civil whistleblower or qui tam actions, and civil monetary penalties laws, among other things, individuals and entities from knowingly presenting, or causing to be presented, to the U.S. government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. government. In addition, the government may assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the U.S. Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

- the U.S. Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals beginning in 2022, and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to the Centers for Medicare and Medicaid Services, or CMS, ownership and investment interests held by the physicians described above and their immediate family members; and

- analogous state and non-U.S. laws and regulations, such as state anti-kickback and false claims laws, which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by the patients themselves; state laws that require pharmaceutical and device companies to comply with the industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and local laws and regulations that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; state and local laws which require the registration of pharmaceutical sales representatives.

Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities may conclude that our business practices, including our relationships with certain physicians, some of whom are compensated in the form of stock options for consulting services provided, do not comply with current or future statutes, regulations, agency guidance or case law involving applicable healthcare laws. If our operations are found to be in violation of any of these or any other health regulatory laws that may apply to us, we may be subject to significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other U.S. healthcare programs, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data, such as information that we may collect in connection with clinical trials in the U.S. and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards can be high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the U.S., HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information on covered entities (defined as health plans, health care clearinghouses and certain health care providers) and their respective business associates, individuals or entities that create, received, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HIPAA mandates the reporting of certain breaches of health information to HHS, affected individuals and if the breach is large enough, the media. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information, a complaint about privacy practices or an audit by HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Even when HIPAA does not apply, according to the Federal Trade Commission or the FTC, failing to take appropriate

steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act, or the FTCA, 15 U.S.C § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. The FTC's guidance for appropriately securing consumers' personal information is similar to what is required by the HIPAA Security Rule.

Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. In addition, California enacted the California Consumer Privacy Act (CCPA) on June 28, 2018, which went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal data. 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. The CCPA may increase our compliance costs and potential liability, and many similar laws have been proposed at the federal level and in other states. In the event that we are subject to or affected by HIPAA, the CCPA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

In Europe, the European Union General Data Protection Regulation (GDPR) went into effect in May 2018 and introduces strict requirements for processing the personal data of EU data subjects. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements. We are also subject to evolving EU laws on data export, as we may transfer personal data from the EU to other jurisdictions. Following Brexit, we will have to comply with the GDPR and the UK GDPR, each regime having the ability to fine up to the greater of €20 million/ £17 million or 4% of global turnover. The relationship between the UK and the EU in relation to certain aspects of data protection law remains unclear, e.g. how data transfers between EU member states. These changes will lead to additional costs and increase our overall risk.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, CROs, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

We have received orphan drug designation for PBCAR0191 for the treatment of ALL, PBCAR20A for the treatment of mantle cell lymphoma, or MCL, and PBCAR269A for the treatment of multiple myeloma, and we may seek orphan drug designation for some or all of our other product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug designation, which may negatively impact our ability to develop or obtain regulatory approval for such product candidates and may reduce our revenue if we obtain such approval.

We may seek orphan drug designation for some or all of our product candidates in specific orphan indications in which there is a medically plausible basis for the use of these products. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a biologics license application, or BLA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. We have received orphan drug designation in the United States for PBCAR0191 for the treatment of ALL. Although we may seek orphan product designation for some or all of our other product candidates, we may never receive such designations.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a BLA, to market the same biologic for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan product exclusivity or if FDA finds that the holder of the orphan drug exclusivity has not shown that it can ensure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Even if we or our collaborators obtain orphan drug designation for a product candidate, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Exclusive marketing rights in the United

States may be limited if we or our collaborators seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if a product obtains orphan drug exclusivity, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Furthermore, the FDA can waive orphan exclusivity if we or our collaborators are unable to manufacture sufficient supply of the product.

Similarly, in Europe, a medicinal product may receive orphan designation under Article 3 of Regulation (EC) 141/2000. This applies to products that are intended for a life-threatening or chronically debilitating condition and either (1) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (2) the product, without the benefits derived from orphan status, would be unlikely to generate sufficient returns in the EU to justify the necessary investment. Moreover, in order to obtain orphan designation in the EU it is necessary to demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU or, if such a method exists, the product will be of significant benefit to those affected by the condition. In the EU, orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and applicants can benefit from specific regulatory assistance and scientific advice. Products receiving orphan designation in the EU can receive 10 years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. However, the 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation—for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the first applicant consents to a second orphan medicinal product application; or
- the first applicant cannot supply enough orphan medicinal product.

If we or our collaborators do not receive or maintain orphan drug designation for product candidates for which we seek such designation, it could limit our ability to realize revenues from such product candidates.

We may seek fast track designation, breakthrough therapy designation, Regenerative Medicine Advanced Therapy, or RMAT, designation, or priority review from the FDA or access to the PRIME scheme from the EMA for some or all of our product candidates, but we may not receive such designations, and even if we do, it may not lead to a faster development or regulatory review or approval process, and will not increase the likelihood that such product candidates will receive marketing approval.

We may seek fast track designation, breakthrough therapy designation, Regenerative Medicine Advanced Therapy, or RMAT, designation or priority review from the FDA, or access to the PRIME scheme from the EMA for some or all of our product candidates. If a drug is intended for the treatment of a serious or life-threatening condition or disease, and nonclinical or clinical data demonstrate the potential to address an unmet medical need, the product may qualify for FDA fast track designation, for which sponsors must apply. The FDA has broad discretion whether or not to grant this designation. If granted, fast track designation makes a drug eligible for more frequent interactions with FDA to discuss the development plan and clinical trial design, as well as rolling review of the application, which means that the company can submit completed sections of its marketing application for review prior to completion of the entire submission. Products with fast track designation may also be eligible for accelerated approval and priority review, if the relevant criteria are met.

Breakthrough therapy designation is intended to expedite the development and review of product candidates that treat serious or life-threatening diseases when "preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development." The designation of a product candidate as a breakthrough therapy provides the same potential benefits as a fast track designation, with more intensive FDA guidance on an efficient development program and an organizational commitment at FDA involving senior managers.

A company may also request RMAT designation of its product candidate, which designation may be granted if the drug meets the following criteria: (1) it qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. Like breakthrough therapy designation, RMAT

designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate, and potential eligibility for rolling review and priority review. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. RMAT- designated products that receive accelerated approval may, as appropriate, fulfill their post-approval requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence (such as electronic health records); through the collection of larger confirmatory data sets; or via post-approval monitoring of all patients treated with such therapy prior to approval of the therapy.

PRIME is a scheme provided by the EMA to enhance support for the development of medicines that target an unmet medical need. To qualify for PRIME, product candidates require early clinical evidence that the therapy has the potential to offer a therapeutic advantage over existing treatments or benefits patients without treatment options. Among the benefits of PRIME are the appointment of a rapporteur to provide continuous support and help build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

There is no assurance that we will obtain fast track designation, breakthrough therapy designation, RMAT designation or access to PRIME for any of our product candidates. Fast track designation, breakthrough therapy designation, RMAT designation and PRIME eligibility do not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval or that the approved indication will not be narrower than the indication covered by the fast track designation, breakthrough therapy designation, RMAT designation or PRIME eligibility. Additionally, fast track designation, breakthrough therapy designation, RMAT designation and access to PRIME can each be revoked if the criteria for eligibility cease to be met as clinical data emerges.

If the product candidates that we or our collaborators may develop receive regulatory approval in the United States or another jurisdiction, they may never receive approval in other jurisdictions, which would limit market opportunities for such product candidate and adversely affect our business.

Approval of a product candidate in the United States by the FDA or by the requisite regulatory agencies in any other jurisdiction does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions. The approval process varies among countries and may limit our or our collaborators' ability to develop, manufacture, promote and sell product candidates internationally. Failure to obtain marketing approval in international jurisdictions would prevent the product candidates from being marketed outside of the jurisdictions in which regulatory approvals have been received. In order to market and sell product candidates in the EU and many other jurisdictions, we and our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and may involve additional preclinical studies or clinical trials both before and after approval. In many countries, any product candidate for human use must be approved for reimbursement before it can be approved for sale in that country. In some cases, the intended price for such product is also subject to approval. Further, while regulatory approval of a product candidate in one country does not ensure approval in any other country, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. If we or our collaborators fail to comply with the regulatory requirements in international markets or to obtain all required marketing approvals, the target market for a particular potential product will be reduced, which would limit our ability to realize the full market potential for the product and adversely affect our business.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize any product candidates we or our collaborators develop and may adversely affect the prices for such product candidates.

In the United States and certain non-U.S. jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our or our collaborators' ability to profitably sell any product candidates that obtain marketing approval.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively the Affordable Care Act, was enacted in the United States. Among the provisions of the Affordable Care Act of importance to our product candidates, the Affordable Care Act established an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, extended manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, expanded eligibility criteria for Medicaid programs, expanded the entities eligible for discounts under the Public Health program, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, created a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D, and created a licensure framework for follow-on biologic products.

On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or Texas District Court Judge, ruled that the entire Affordable Care Act is invalid based primarily on the fact that the TCJA enacted on December 22, 2017, repealed the tax-based shared responsibility payment imposed by the Affordable Care Act, on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate". On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. It is unclear how these decisions, subsequent appeals, if any, or other efforts to challenge, repeal or replace the Affordable Care Act will impact the law or our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute will remain in effect through 2029 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny recently over pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies, rebates and price negotiation for pharmaceutical products, some of which are included in the Trump administration's budget proposals for fiscal years 2019 and 2020, as well as recent bills introduced by the U.S. Senate and House of Representatives, respectively. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services has begun soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. Although a number of these, and other potential measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product and medical device pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and medical devices to purchase and which suppliers will be included in their prescription drug and other healthcare programs.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a framework for certain patients with life-threatening diseases or conditions to access certain investigational new drug 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 products available to eligible patients as a result of the Right to Try Act.

We expect that the Affordable Care Act, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we or our collaborators may receive for any approved or cleared product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we or our collaborators are slow or unable to adapt to new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, any of our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Even if we obtain regulatory approval for any products that we develop alone or with collaborators, such products will remain subject to ongoing regulatory requirements, which may result in significant additional expense.

Even if products we develop alone or with collaborators receive regulatory approval, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, distribution, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information, among other things. Any regulatory approvals received for such products may also be subject to limitations on the approved indicated uses for which they may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing and surveillance studies. For example, the holder of an approved BLA in the United States is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. FDA guidance advises that patients treated with some types of gene therapy undergo follow-up observations for potential adverse events for as long as 15 years. Similarly, in the EU, pharmacovigilance obligations are applicable to all medicinal products. In addition to those, holders of a marketing authorization for gene or cell therapy products must detail, in their application, the measures they envisage to ensure follow-up of the efficacy and safety of these products. In cases of particular concern, marketing authorization holders for gene or cell therapy products in the EU may be required to design a risk management system with a view to identifying, preventing or minimizing risks and may be obliged to carry out post-marketing studies. In the United States, the holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Similar provisions apply in the EU. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws. Similarly, in the EU any promotion of medicinal products is highly regulated and, depending on the specific jurisdiction involved, may require prior vetting by the competent national regulatory authority.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the BLA or foreign marketing application. If we, our collaborators or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory agency may impose restrictions relative to that product, the manufacturing facility or us or our collaborators, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

Moreover, if any of our product candidates are approved, our product labeling, advertising, promotion and distribution will be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling.

If we or our collaborators fail to comply with applicable regulatory requirements following approval of any potential products we may develop, authorities may:

- issue an untitled enforcement letter or a warning letter asserting a violation of the law;
- seek an injunction, impose civil and criminal penalties, and impose monetary fines, restitution or disgorgement of profits or revenues;
- suspend or withdraw regulatory approval;
- suspend or terminate any ongoing clinical trials or implement requirements to conduct post-marketing studies or clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our collaborators;
- restrict the labeling, marketing, distribution, use or manufacturing of products;
- seize or detain products or otherwise require the withdrawal or recall of products from the market;
- refuse to approve pending applications or supplements to approved applications that we or our collaborators submit;
- refuse to permit the import or export of products; or
- refuse to allow us or our collaborators to enter into government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our or our collaborators' ability to commercialize products and our ability to generate revenues.

In addition, the FDA's policies, and policies of foreign regulatory agencies, may change, and additional regulations may be enacted that could prevent, limit or delay regulatory approval of product candidates. For example, in December 2016, the 21st Century Cures Act, or the Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of biologics and spur innovation, but its ultimate implementation is unclear. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance and review and approval of marketing applications. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose restrictions on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements, or if we or our collaborators are unable to maintain regulatory compliance, marketing approval that has been obtained may be lost and we may not achieve or sustain profitability.

Even if any product we develop alone or with collaborators receives marketing approval, such product may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

The commercial success of any potential therapeutic products we develop alone or with collaborators will depend upon their degree of market acceptance by physicians, patients, third-party payors and others in the medical community. Even if any potential therapeutic products we develop alone or with collaborators receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. The degree of market acceptance of any product we develop alone or with collaborators, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product as demonstrated in clinical trials;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved by FDA, the EMA or other regulatory authorities;
- product labeling or product insert requirements of the FDA, the EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- public attitudes regarding genome editing technologies;
- our and any collaborators' ability to educate the medical community about the safety and effectiveness of the product;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, as well as their willingness to accept a therapeutic intervention that involves the editing of the patient's genome;
- the potential and perceived advantages compared to alternative treatments;
- convenience and ease of administration compared to alternative treatments;
- any restrictions on the use of such product together with other treatments or products;
- market introduction of competitive products;
- publicity concerning such product or competing products and treatments;
- the ability to offer such product for sale at a competitive price;
- the strength of marketing and distribution support; and
- sufficient third-party coverage and adequate reimbursement.

If any products we develop alone or with collaborators do not achieve an adequate level of acceptance, we may not generate significant product revenues, and we may not become profitable.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any products we develop alone or with collaborators, the commercialization of such products may not be successful if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of biopharmaceutical or other commercial products. To achieve commercial success for any approved products for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, certain product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, restricted or closed distribution channels may make it difficult to distribute products to segments of the patient population, and the lack of complementary medicines to be offered by sales personnel may put us at a competitive disadvantage relative to companies with more extensive product lines.

Recruiting and training a sales force or reimbursement specialists are expensive and time consuming and could delay any product launch. If the commercial launch of a product for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses, and our investment would be lost if we cannot retain or reposition our commercialization personnel. Factors that may inhibit our efforts to commercialize products on our own include:

- unforeseen costs and expenses associated with creating an independent commercialization organization;
- our inability to recruit, train, retain and effectively manage adequate numbers of effective sales, marketing, customer service and other support personnel, including for reimbursement or medical affairs;
- the inability of sales personnel to educate adequate numbers of physicians on the benefits of our future medicines; and
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors.

If we choose to enter into arrangements with third parties to perform sales, marketing, commercial support or distribution services, we may not be successful in entering into such arrangements or may be unable to do so on terms that are favorable to us. Entering into such third-party arrangements may subject us to a variety of risks, including:

- product revenues or profitability to us being lower than if we were to market and sell any products we or our collaborators may develop ourselves;
- our inability to exercise direct control over sales and marketing activities and personnel;
- failure of the third parties to devote necessary resources and attention to, or other inability to, sell and market any products we or our collaborators may develop;
- potential disputes with third parties concerning sales and marketing expenses, calculation of royalties and sales and marketing strategies; and
- unforeseen costs and expenses associated with sales and marketing.

If we do not establish effective commercialization capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any of our product candidates that may receive approval.

If the market opportunities for any products we develop alone or with collaborators are smaller than our estimates, or if we are unable to successfully identify enough patients, our revenues may be adversely affected.

We focus some of our research and product development on treatments for rare genetic diseases. Our and our collaborators' projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with product candidates we may develop, are based on estimates. These estimates may prove to be incorrect, and new studies may change the estimated incidence or prevalence of these diseases. The number of patients in the United States, Europe and elsewhere may turn out to be lower than expected, and patients may not be amenable to treatment with products that we may develop alone or with collaborators, or may become increasingly difficult to identify or gain access to, any of which would decrease our ability to realize revenue from any such products for such diseases.

The successful commercialization of potential products will depend in part on the extent to which governmental authorities and health insurers establish coverage, and the adequacy of reimbursement levels and pricing policies, and failure to obtain or maintain coverage and adequate reimbursement for any potential products that may receive approval, could limit marketability of those products and decrease our ability to generate revenue.

The availability of coverage and adequacy of reimbursement by government healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors is essential for most patients to be able to afford prescription medications such as the potential therapeutic products we develop alone or with collaborators. The ability to achieve acceptable levels of coverage and reimbursement for any potential products that may be approved by governmental authorities will have an effect on our and our collaborators' ability to successfully commercialize such products. Even if products we develop alone or with collaborators obtain coverage by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. If coverage and reimbursement in the United States, the EU or elsewhere is not available for any products we develop alone or with collaborators that may be approved, or any reimbursement that may become available is decreased or eliminated in the future, we and our collaborators may be unable to commercialize such products.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved drugs and biologics. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. In August 2019, the CMS published its decision to cover autologous treatment for cancer with T-cells expressing at least one CAR when administered at healthcare facilities enrolled in the FDA risk evaluation and mitigation strategies and used for an FDA-approved indication or for other uses when the product has been FDA-approved and the use is supported in one or more CMS-approved compendia. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for any product that we develop alone or with collaborators.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us or our collaborators to provide scientific and clinical support for the use of any potential products that may be approved to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice. Obtaining coverage and adequate reimbursement for products we develop alone or with collaborators may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. In certain instances, payors may not separately reimbursement for the product itself, but only for the treatments or procedures in which such product is used. A decision by a third-party payor not to cover or separately reimburse for products that we develop alone or with collaborators or procedures using such products, could reduce physician utilization of any such products that may receive approval.

Third-party payors are increasingly challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. If approved, it is possible that a third-party payor may consider any products that we develop alone or with collaborators as substitutable and only offer to reimburse patients for the less expensive product. Pricing of existing third-party therapeutics may limit the amount we will be able to charge for any products that may receive approval even if we or our collaborators show improved efficacy or improved convenience of administration such products. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in the product. If reimbursement is not available or is available only at limited levels, we or our collaborators may not be able to successfully commercialize any of the products that we develop, even if approved, and we may not be able to obtain a satisfactory financial return on them. Moreover, increasing efforts by governmental and third-

party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for any products we develop alone or with collaborators that may receive approval. We expect to experience pricing pressures in connection with the sale of any products that may receive approval due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and elsewhere have and will continue to put pressure on the pricing and usage of any products we develop alone or with collaborators that may receive approval. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional international price controls or other changes in pricing regulation could restrict the amount that we or our collaborators are able to charge for products that we develop that may receive approval. Accordingly, in markets outside the United States, the reimbursement for such products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

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

If we are successful in achieving regulatory approval to commercialize any biologic product candidate we develop alone or with collaborators, it may face competition from biosimilar products. In the United States, our product candidates are regulated by the FDA as biologic products subject to approval under the BLA pathway. The Biologics Price Competition and Innovation Act of 2009, or the BPCIA, created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products following the approval of an original BLA. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product may not be submitted until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years after the reference product was first licensed by the FDA. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for biological product candidates.

We believe that any of our product candidates that are approved as biological products under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider such product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar product, once approved, will be substituted for any one of our or our collaborators' reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. If competitors are able to obtain marketing approval for biosimilars referencing any products that we develop alone or with collaborators that may be approved, such products may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences.

Additional Risks Related to the Identification, Development and Commercialization of Our Food and Agricultural Product Candidates

The regulatory landscape that may govern any potential food or agricultural products that we or our collaborators may develop is uncertain and may adversely impact the development and commercialization activities of our food platform.

In the United States, the United States Department of Agriculture, or the USDA, regulates, among other things, the introduction (including the importation, interstate movement or release into the environment) of organisms and products altered or produced through genetic engineering determined to be plant pests or for which there is reason to believe are plant pests. Such organisms and products are considered "regulated articles." However, a petitioner may submit a request for a determination by the USDA of "nonregulated status" for a particular article. A petition for determination of nonregulated status must include detailed information, including relevant experimental data and publications, field trial reports and a description of the genotypic differences between the regulated article and the nonmodified recipient organism, among other things. Neither we nor, to our knowledge, our collaborators

have obtained a determination from the USDA that any product candidates are not "regulated articles" under these regulations. We cannot predict whether the USDA, advocacy groups or other third parties will contend that these products are regulated articles. The USDA's regulations also require that companies obtain a permit or file a notification before engaging in the introduction (including the importation, interstate movement or release into the environment such as in field trials) of "regulated articles." Additionally, a change in the way the USDA interprets its regulations, or a change in its regulations, could subject our or our collaborators' products to more burdensome regulations, thereby substantially increasing the time and costs associated with developing product candidates. Complying with the USDA's Part 340 regulations, including permitting requirements, is a costly, time-consuming process and could delay or prevent the commercialization of any potential food or agricultural products we or our collaborators may develop.

Any potential food or agricultural products that we or our collaborators develop may also be subject to extensive FDA food product regulations. Under sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act, or the FDCA, any substance that becomes or is reasonably expected to become a component of food is a food additive and is therefore subject to FDA premarket review and approval, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use (generally recognized as safe, or GRAS), or unless the use of the substance is otherwise excluded from the definition of a food additive, and any food that contains an unsafe food additive is considered adulterated under section 402(a)(2)(C) of the FDCA. The FDA may classify some or all of the potential food or agricultural products that we or our collaborators may develop as containing a food additive that is not GRAS or otherwise determine that such products contain significant compositional differences from existing plant products that require further review. Such classification would cause these potential products to require pre-market approval, which could delay the commercialization of these products. In addition, the FDA is currently evaluating its approach to the regulation of gene-edited plants. For example, on January 19, 2017, the FDA issued a notice in the Federal Register requesting public comment on the use of genome editing techniques to produce new plant varieties that are used for human or animal food or foods that are derived from such new plant varieties produced using genome editing. Among other things, the notice asked for data and information in response to questions about the safety of foods from gene-edited plants, such as whether categories of gene-edited plants present food safety risks different from other plants produced through traditional plant breeding. If the FDA enacts new regulations or policies with respect to gene-edited plants, such policies could result in additional compliance costs and delay or even prevent the commercialization of any of our product candidates, which could negatively affect our profitability. Any delay in the regulatory consultation process, or a determination that any potential products we or our collaborators may develop do not meet regulatory requirements by the FDA or other regulators, could cause a delay in, or prevent, the commercialization of our products, which may lead to reduced acceptance by the public and an increase in competitor products that may directly compete with ours, or could otherwise negatively impact our business, prospects and results of operations.

On May 4, 2018, the USDA issued a proposed rule implementing the National Bioengineered Food Disclosure Standard, with a proposed compliance date of January 1, 2020. Under this proposed rule, the label of a bioengineered, or BE, food must include a disclosure that the food is a BE food or contains a BE ingredient, with certain exceptions. This proposed rule defines BE food as "a food that contains genetic material that was has been modified through in vitro recombinant deoxyribonucleic acid, or DNA, techniques and for which the modification could not otherwise be obtained through conventional breeding or found in nature," except in the case of an incidental additive present in food at an insignificant level and that does not have any technical or functional effect in the food. If this proposed rule is passed and products developed by our collaborators based on our ARCUS technology are required to be labeled "BE," consumer perception of these products may be adversely affected.

In the EU, genetically modified foods, or GM foods, can only be authorized for sale on the market once they have been subject to rigorous safety assessments. The procedures for evaluation and authorization of GM foods are governed by Regulation (EC) 1829/2003 on GM food and feed and Directive 2001/18/EC on the release of genetically modified organisms, or GMOs, into the environment. If the GMO is not to be used in food or feed, then an application must be made under Directive 2001/18/EC. If the GMO is to be used in food or feed (but it is not grown in the EU) then a single application for both food and feed purposes under Regulation 1829/2003 should be made. If the GMO is used in feed or food and it is also grown in the EU, an application for both cultivation and food/feed purposes needs to be carried out under Regulation (EC) 1829/2003. A different EU regulation, Regulation (EC) 1830/2003, regulates the labeling of products that contain GMOs that are placed on the EU market. Directive 2001/18/EC was amended by Directive (EU) 2015/412 which gives EU Member States more flexibility to allow, restrict or prohibit growing GMOs in their territory, on a range of environmental grounds, even if such crops were previously authorized at EU level. Under Directive 2015/412, EU Member State restrictions or prohibitions can only cover cultivation, and not the free circulation and import of genetically modified seeds and plant propagation material, and should be in conformity with the internal market rules of the EU Treaties. In March 2018, the Commission adopted Commission Directive (EU) 2018/350 amending Directive 2001/18/EC as regards the environmental risk assessment of GMOs. This measure aims to bring the assessment of the environmental risk of GM foods in the EU up to date with developments in scientific knowledge and technical progress. Member States have to transpose the Directive by September 29, 2019. Further EU level legislation on GM foods includes Directive 2009/41/EC on contained use of genetically modified micro-organisms and Regulation (EC) 1946/2003 on transboundary movements of GMOs.

We cannot predict whether or when any governmental authority will change its regulations with respect to any potential food or agricultural products that we develop alone or with collaborators. Advocacy groups have engaged in publicity campaigns and filed lawsuits in various countries against companies and regulatory authorities seeking to halt biotechnology approval activities or influence public opinion against genetically engineered products. In addition, governmental reaction to negative publicity concerning genetically edited agricultural products could result in greater regulation of genetic research and derivative products or regulatory costs that render our or our collaborators' development of potential food or agricultural products cost prohibitive. Our collaborators may use or integrate our products or technology into other products in ways that could subject those collaborators or products to additional regulation.

The overall agricultural industry is susceptible to agricultural price changes, and we may be exposed to risks from changes in commodity prices.

Changes in the prices of agricultural products could result in changes in demand for and prices of food and agricultural products that we or our collaborators may develop. We may be susceptible to these changes as a result of factors beyond our control, such as general economic conditions, seasonal fluctuations, weather conditions, demand, food safety concerns, product recalls and government regulations, subsidies or market export tariffs. If demand for agricultural products that we or our collaborators may develop is negatively impacted, our potential revenues under collaboration agreements for such products may decline, which could adversely affect our results of operations.

The successful commercialization of any food or agricultural products we develop will depend in part on our collaborators' ability to produce high-quality plants and seeds cost-effectively on a large scale and to accurately forecast demand for such potential products, and they may be unable to do so.

The production of commercial-scale quantities of food or agricultural products or seeds for them requires the multiplication of the plants or seeds through a succession of plantings and seed harvests. The cost-effective production of high-quality, high-volume quantities of such products or seeds may depend in part on our collaborators' abilities to scale production processes to produce plants and seeds in sufficient quantity to meet demand. Our collaborators' existing or future plant and seed production techniques may not enable timely meeting of large-scale production goals cost-effectively for any potential food or agricultural products that we and our collaborators may develop. Although we have worked with some of the largest plant biotechnology companies to edit gene targets and develop potential product candidates in a variety of crop plants, no commercial food or agricultural products have ever been developed using our technology.

In addition, because of the length of time it takes to produce commercial quantities of marketable plants and seeds, our collaborators will need to make seed production decisions well in advance of food product sales. The ability to accurately forecast demand can be adversely affected by a number of factors outside of their control, including changes in market conditions, environmental factors, such as pests and diseases, and adverse weather conditions.

The commercial success of any consumer-centric food or agricultural products that we or our collaborators may develop is reliant on the needs of food manufacturers and the recognition of shifting consumer preferences.

The commercial success of any consumer-centric products depends in part on the ability of the food manufacturer to accurately determine the shifting needs and desires of the ultimate consumer. We will not control the marketing, distribution labeling or any other aspects of the sale and commercialization of the manufacturers' food products. Consumer preferences may be a significant driver in the success of food manufacturers in their efforts to sell food and agricultural products, including products that we or our collaborators may develop. While current trends indicate that consumer preferences may be moving towards "healthier" options, we cannot predict whether such trends will continue or which types of food products will be demanded by consumers in the future. Additionally, as health and nutritional science continues to progress, consumer perception of what foods, nutrients and ingredients are considered "healthy" may shift. We and our collaborators may not be dynamic enough in responding to consumer trends and creating products that will be demanded by consumers in the future. In addition, if consumer demand is lower than our estimates or those of our collaborators, our ability to realize revenues from potential food or agricultural products may be limited. Failure by our collaborators to successfully recognize consumer trends could lower demand for potential food or agricultural products that we or our collaborators may develop, which could harm our business, results of operations and financial condition.

Some of the potential food products we develop alone or with collaborators may be distributed into markets or countries in which they have not received regulatory approval, which may result regulatory challenges or lawsuits.

The scale of the agricultural industry may make it difficult to monitor and control the distribution of any potential food products that we develop alone or with collaborators. As a result, such products may be sold inadvertently within jurisdictions where they are not approved for distribution. Such sales may lead to regulatory challenges or lawsuits against us, which could result in significant expenses and divert our management's attention, which could harm our business, results of operations and financial condition.

Risks Related to Our Reliance on Third Parties

We have entered into significant arrangements with collaborators and expect to depend on collaborations with third parties for certain research, development and commercialization activities, and if any such collaborations are not successful, it may harm our business and prospects.

We have sought in the past, and anticipate that we will continue to seek in the future, third-party collaborators for the research, development and commercialization of certain product candidates and the research and development of certain technologies. For example, we are party to the Servier Agreement, pursuant to which we are focused on research and development of allogeneic CAR T cell therapies for up to six oncology targets that utilize or incorporate our genome editing technologies, and we are also party to a collaboration with Gilead focused on research and development of therapeutic product candidates for the treatment of Hepatitis B using ARCUS nucleases. In addition, our food platform is based on a consumer-centric model, whereby our research and development activities and potential revenues are based on the needs and commercial success of our collaborators. For example, we are a party to a commercial license agreement with Cargill focused on targeting and modifying certain genes related to saturated oil production in canola plants. Our likely collaborators for other product research and development arrangements include large and mid-size pharmaceutical and biotechnology companies biotechnology and food, beverage, nutrition and agricultural biotechnology companies, and our likely collaborators for other technology research and development arrangements include universities and other research institutions.

Working with collaborators poses several significant risks. We have limited control over the amount and timing of resources that our collaborators dedicate to the product candidates or technologies we may seek to develop with them. A variety of factors may impact resource allocation decisions of collaborators, such as study or trial results, changes in the collaborator's strategic focus, turnover in personnel responsible for the development activities, financial capacity or external factors such as a business combination or change in control that diverts resources or creates competing priorities. Collaboration agreements may not lead to development or commercialization of product candidates or the development of technologies in the most efficient manner or at all. Resource allocation and other developmental decisions made by our collaborators may result in the delay or termination of research programs, studies or trials, repetition of or initiation of new studies or trials or provision of insufficient funding or resources for the completion of studies or trials or the successful marketing and distribution of any product candidates that may receive approval. Collaborators could independently develop, or develop with third parties, product candidates or technologies that compete directly or indirectly with our product candidates or technologies if the collaborators believe that competitive products or technologies are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours. Collaborators may not properly obtain, maintain, enforce or defend our intellectual property or proprietary rights or may use our proprietary information in such a way that could jeopardize or invalidate our proprietary information or expose us to potential litigation. Disputes may arise between us and our collaborators that result in the delay or termination of the research, development or commercialization activities or that result in costly litigation or arbitration that diverts management attention and resources.

Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. If our collaborations do not result in the successful development and commercialization of product candidates or technologies, or if one of our collaborators terminates its agreement with us, we may not receive any future funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of product candidates or technologies could be delayed, and we may need additional resources to develop such product candidates or technologies. In addition, if one of our collaborators terminates its agreement with us, we may be unable to find a suitable replacement collaborator or any replacement collaborator or attract new collaborators and may need to raise additional capital to pursue further development or commercialization of the applicable product candidates or technologies. These events could delay development programs, negatively impact the perception of our company in business and financial communities or cause us to have to cease development of the product candidate covered by the collaboration arrangement. Failure to develop or maintain relationships with any current collaborators could result in the loss of opportunity to work with that collaborator or reputational damage that could impact our relationships with other collaborators in the relatively small industry communities in which we operate. Moreover, all of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K apply to the activities of our collaborators. If our existing collaboration agreements or any collaborative or strategic relationships we may establish in the future are not effective and successful, it may damage our reputation and business prospects, delay or prevent the development and commercialization of product candidates and inhibit or preclude our ability to realize any revenues.

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

Our research and product development programs and the potential commercialization of any product candidates we develop alone or with collaborators will require substantial additional cash to fund expenses, and we expect that we will continue to seek collaborative arrangements with others in connection with the development and potential commercialization of current and future product candidates or the development of ancillary technologies. We face significant competition in establishing relationships with appropriate collaborators. 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. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include, among other things and as applicable for the type of potential product or technology, an assessment of the opportunities and risks of our technology, the design or results of studies or trials, the likelihood of approval, if necessary, by the USDA, the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products and technologies and industry and market conditions generally.

Current or future collaborators may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us. Additionally, we may be restricted under existing collaboration agreements from entering into future agreements on certain terms or for certain development activities with potential collaborators. For example, we have granted exclusive rights or options to Servier and Gilead for certain targets, and during the terms of our respective collaboration agreements with them we will be restricted from granting rights to other parties to use our ARCUS technology to pursue potential products that address those targets. Similarly, our collaboration agreements have in the past and may in the future contain non-competition provisions that could limit our ability to enter into strategic collaborations with future collaborators.

Collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we do enter into additional collaboration agreements, the negotiated terms may force us to relinquish rights that diminish our potential profitability from development and commercialization of the subject product candidates or others. If we are unable to enter into additional collaboration agreements, we may have to curtail the research and development of the product candidate or technology for which we are seeking to collaborate, reduce or delay research and development programs, delay potential commercialization timelines, reduce the scope of any sales or marketing activities or undertake research, development or commercialization activities at our own expense. If we elect to increase our expenditures to fund research, 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.

We expect to rely on third parties to conduct, supervise and monitor our clinical trials and some aspects of our research and preclinical testing, and if those third parties do not successfully carry out their contractual duties, comply with regulatory requirements, or otherwise perform in a satisfactory manner, we may not be able to obtain regulatory approval or commercialize product candidates, or such approval or commercialization may be delayed, and our business may be substantially harmed.

We may rely on medical institutions, universities, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct preclinical studies and future clinical trials for our product candidates. Nevertheless, we will be responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on such third parties will not relieve us of our regulatory responsibilities.

Although we intend to design the trials for our product candidates either alone or with collaborators, third parties may conduct all of the trials. As a result, many important aspects of our research and development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future studies and trials will also result in less direct control over the management of data developed through studies and trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes and difficulties in coordinating activities. Outside parties may have staffing difficulties, fail to comply with contractual obligations, experience regulatory compliance issues, undergo changes in priorities, become financially distressed or form relationships with other entities, some of which may be our competitors. We also face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs or other third parties, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. For any violations of laws and regulations during the conduct of our preclinical studies and future clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulations, commonly referred to as Good Clinical Practices, or GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. If we, our collaborators, our CROs or other third parties fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We also are required to register certain ongoing clinical trials and post the results of such completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

If our CROs or other third parties do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, trials for product candidates may be extended, delayed or terminated, and we or our collaborators may not be able to obtain regulatory approval for, or successfully commercialize, any product candidate that we develop. If we are required to repeat, extend the duration of or increase the size of any trials we conduct, it could significantly delay commercialization and require significantly greater expenditures. As a result of any of these factors, our financial results and the commercial prospects for any product candidate that we or our collaborators may develop would be harmed, our costs could increase and our ability to generate revenues could be delayed.

We expect to rely on third parties to supply raw materials or manufacture product supplies that are necessary for the conduct of preclinical studies, clinical trials and manufacturing of our product candidates, and failure by third parties to provide us with sufficient quantities of products, or to do so at acceptable quality levels or prices and on a timely basis, could harm our business.

We are dependent on third parties for the supply of various biological materials, such as cells, cytokines and antibodies, and the manufacture of product supplies, such as media, plasmids, mRNA and AAV viral vectors, that are necessary to produce our product candidates. The supply of these materials could be reduced or interrupted at any time. In such case, identifying and engaging an alternative supplier or manufacturer could result in delay, and we may not be able to find other acceptable suppliers or manufacturers on acceptable terms, or at all. Switching suppliers or manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. If we change suppliers or manufacturers for commercial production, applicable regulatory agencies may require us to conduct additional studies or trials. If key suppliers or manufacturers are lost, or if the supply of the materials is diminished or discontinued, we or our collaborators may not be able to develop, manufacture and market product candidates in a timely and competitive manner, or at all. If any of our product candidates receives approval, we will likely need to seek alternative sources of supply of raw materials or manufactured product supplies and there can be no assurance that we will be able to establish such relationships to provide such supplies on commercially reasonable terms or at acceptable quality levels, if at all. If we are unable to identify and procure additional sources of supply that fit our required needs, we could face substantial delays or incur additional costs in procuring such materials. In addition, manufactured product supplies are subject to stringent manufacturing processes and rigorous testing. Delays in the completion and validation of facilities and manufacturing processes of these materials could adversely affect the ability to complete studies or trials and commercialize any product candidates that may receive approval. Furthermore, if our suppliers or manufacturers encounter challenges relating to employee turnover, the supply and manufacturing of our materials could be delayed or adversely affected as such parties seek to hire and train new employees. These factors could cause the delay of studies or trials, regulatory submissions, required approvals or commercialization of product candidates that we or our collaborators may develop, cause us to incur higher costs and prevent us from commercializing products successfully. Furthermore, if our suppliers or manufacturers fail to meet contractual requirements, and we are unable to secure one or more replacements capable of production at a substantially equivalent cost, our or our collaborators' studies or trials may be delayed and we could lose potential revenue.

We may rely on third parties for at least a portion of the manufacturing process of product candidates, and failure by those parties to adequately perform their obligations could harm our business.

While we expect to use our MCAT facility for certain of our clinical-scale manufacturing and processing needs, we may continue to rely on outside vendors for at least a portion of the manufacturing process of product candidates that we or our collaborators may develop. The facilities used by our contract manufacturers to manufacture product candidates must be approved by the FDA or other foreign regulatory agencies pursuant to inspections that will be conducted after we submit an application to the FDA or other foreign regulatory agencies. To the extent that we or our collaborators engage third parties for manufacturing services, we will not control the manufacturing process of, and will be completely dependent on, our contract manufacturing providers for compliance with cGMP requirements for manufacture of the product candidates. We have not yet caused any product candidates to be manufactured or processed on a commercial scale and may not be able to do so. We will make changes as we work to optimize the manufacturing process, and we cannot be sure that even minor changes in the process will result in products that are safe and effective. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market any of our or our collaborators' potential products.

Risks Related to Intellectual Property

Our ability to compete may decline if we do not adequately protect our proprietary rights, and if our proprietary rights do not provide a competitive advantage.

Our commercial success depends upon obtaining and maintaining proprietary rights to our intellectual property estate, including rights relating to ARCUS and to our product candidates, as well as successfully defending these rights against third-party challenges and successfully enforcing these rights to prevent third-party infringement. We will only be able to protect ARCUS and product candidates from unauthorized use by third parties to the extent that valid and enforceable patents cover them. Our ability to obtain and maintain patent protection for ARCUS and our product candidates is uncertain due to a number of factors, including that:

- we may not have been the first to invent the technology covered by our pending patent applications or issued patents;
- we may not be the first to file patent applications covering product candidates, including their compositions or methods of use, as patent applications in the United States and most other countries are confidential for a period of time after filing;
- our compositions and methods may not be patentable;
- our disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;
- any or all of our pending patent applications may not result in issued patents;
- others may independently develop identical, similar or alternative technologies, products or compositions or methods of use thereof;
- others may design around our patent claims to produce competitive technologies or products that fall outside of the scope of our patents;
- we may fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection;
- we may not seek or obtain patent protection in countries that may eventually provide us a significant business opportunity;
- any patents issued to us may not provide a basis for commercially viable products, may not provide any competitive advantages or may be successfully challenged by third parties;
- others may identify prior art or other bases upon which to challenge and ultimately invalidate our patents or otherwise render them unenforceable; and
- the growing scientific and patent literature relating to engineered endonucleases, including our own patents and publications, may make it increasingly difficult or impossible to patent new engineered nucleases in the future.

Even if we have or obtain patents covering ARCUS or any product candidates or compositions, we and our collaborators may still be barred from making, using and selling such product candidates or technologies because of the patent rights of others. Others may have filed, and in the future may file, patent applications covering compositions, products or methods that are similar or identical to ours, which could materially affect our ability to successfully develop any product candidates or to successfully commercialize any approved products alone or with collaborators. In addition, because patent applications can take many years to issue, there may be currently pending applications unknown to us that may later result in issued patents that we or our collaborators may infringe. These patent applications may have priority over patent applications filed by us.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. For example, in August 2019, the Patent Trial and Appeal Board, or the PTAB, of the United States Patent and Trademark Office, or the USPTO, initiated two patent interferences, administrative proceedings within the USPTO, involving a family of patents that have been issued to us and a pending patent application filed by a third party. An interference is conducted by the PTAB when opposing parties have applied for patent claims to the same invention or substantially the

same invention. The interference is conducted to determine which party, if either, is entitled to claims to the subject matter of the interference. An adverse outcome in such proceedings could affect our competitive position, including, without limitation, loss of some or all of our involved patent claims, limiting our ability to stop others from using or commercializing similar or identical technology and products, which could harm our business, financial condition and results of operations. Protecting our patent rights in connection with such proceeding may also be expensive and may involve the diversion of significant management time.

Furthermore, we cannot guarantee that any patents will be issued from any pending or future owned or licensed patent applications. Thus, even if our patent applications issue as patents, they may not issue in a form that will provide us with meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. In addition, third parties may be able to develop products that are similar to, or better than, ours in a way that is not covered by the claims of our patents, or may have blocking patents that could prevent us from marketing our products or practicing our own patented technology. Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however the life of a patent, and the protection it affords, is limited. Without patent protection for current or future product candidates, we may be open to competition from generic versions of such potential products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to those we or our collaborators may develop.

Obtaining and maintaining a patent portfolio entails significant expense, including periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and patent applications. These expenditures can be at numerous stages of prosecuting patent applications and over the lifetime of maintaining and enforcing issued patents. We may or may not choose to pursue or maintain protection for particular intellectual property in our portfolio. If we choose to forgo patent protection or to allow a patent application or patent to lapse purposefully or inadvertently, our competitive position could suffer. There are situations, however, in which failure to make certain payments or noncompliance with certain requirements in the patent process can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Legal action that may be required to enforce our patent rights can be expensive and may involve the diversion of significant management time. There can be no assurance that we will have sufficient financial or other resources to file and pursue infringement claims, which typically last for years before they are concluded. In addition, these legal actions could be unsuccessful and result in the invalidation of our patents, a finding that they are unenforceable or a requirement that we enter into a licensing agreement with or pay monies to a third party for use of technology covered by our patents. We may or may not choose to pursue litigation or other actions against those that have infringed on our patents, or have used them without authorization, due to the associated expense and time commitment of monitoring these activities. If we fail to successfully protect or enforce our intellectual property rights, our competitive position could suffer, which could harm our results of operations.

Many biotechnology companies and academic institutions are currently pursuing a variety of different nuclease systems for genome engineering, such a TAL endonucleases, zinc-finger nucleases, and CRISPR/Cas9 nucleases, and the use of those nucleases in cancer immunotherapy, gene therapy and genome editing. Although those nucleases are physically and chemically different from our ARCUS nucleases, those companies and institutions may seek patents that broadly cover aspects of cancer immunotherapy, gene therapy and genome editing using nucleases generally. Such patents, if issued, valid and enforceable, could prevent us from marketing our product candidates, if approved, practicing our own patented technology, or might require us to take a license which might not be available on commercially reasonable terms or at all. While we expect that we will continue to be able to patent our ARCUS nucleases for the foreseeable future, as the scientific and patent literature relating to engineered endonucleases increases, including our own patents and publications, it may become more difficult or impossible to patent new engineered endonucleases in the future.

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

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. We may need to outsource and rely on third parties for many aspects of the development, sales and marketing of any products covered under our current and future license agreements. Delay or failure by these third parties could adversely affect the continuation of our license agreements with our licensors. If we fail to comply with any of our obligations under these agreements, or we are subject to a bankruptcy, our licensors may have the right to terminate the license, in which event we would not be able to market any products covered by the license.

In addition, disputes may arise regarding the payment of the royalties due to licensors in connection with our exploitation of the rights we license from them. Licensors may contest the basis of royalties we retained and claim that we are obligated to make payments under a broader basis. In addition to the costs of any litigation we may face as a result, any legal action against us could increase our payment obligations under the respective agreement and require us to pay interest and potentially damages to such licensors.

In some cases, patent prosecution of our licensed technology is controlled solely by the licensor. If such licensor fails to obtain and maintain patent or other protection for the proprietary intellectual property we license from such licensor, we could lose our rights to such intellectual property or the exclusivity of such rights, and our competitors could market competing products using such intellectual property. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we or our collaborators may be unable to develop or commercialize the affected product candidates, which could harm our business significantly. In other cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners.

For example, our license agreement with Duke University, or Duke, which we refer to as the Duke License, imposes various payment, royalty and other obligations on us in order to maintain the license. If we fail to make royalty payments or milestone payments required under the Duke License, Duke may terminate the agreement. If we or our affiliates obtain a license from a third party to practice the Duke technology, we must use commercially reasonable efforts to secure a covenant not to sue Duke, or any of its faculty, students, employees or agents, for any research and development efforts conducted at Duke that resulted in the creation of any of its inventions or intellectual property rights arising therefrom. Additionally, because development of the Duke technology was funded in part by the U.S. government, it is subject to certain government rights and obligations, including the requirement that any products sold in the United States based upon such technology be substantially manufactured in the United States.

In addition, our cross-license agreement with Cellectis, or the Cellectis License, imposes various obligations on us in order to maintain the license. In particular, if we participate in or provide assistance to a third party challenging the validity, enforceability and/or patentability of any claim of any patent licensed to us by Cellectis under this agreement, Cellectis may terminate the agreement. The Cellectis License does not provide exclusive rights to use the licensed intellectual property and technology or rights in all relevant fields in which we may wish to develop or commercialize our technology and products in the future. As a result, we are not able to prevent competitors from developing and commercializing competitive products and technology that may use this technology. Additionally, we do not have the right to control the preparation, filing, prosecution, maintenance, enforcement and defense of patents and patent applications covering the technology that we license from Cellectis. Therefore, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained and defended in a manner consistent with the best interests of our business. If Cellectis or other licensors fail to prosecute, maintain, enforce and defend the patents subject to such licenses, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected.

If we fail to comply with our obligations under the Duke License or the Cellectis License, or arrangements with any other licensors, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product candidate that is covered by these agreements, which could materially adversely affect the value of any such product candidate. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

Disputes may arise regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the amounts of royalties, milestones or other payments due to our licensors;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our collaborators; and
- the priority of invention of patented technology.

Such disputes may be costly to resolve and may divert management’s attention away from day-to-day activities. If disputes over intellectual property that we have licensed from third parties prevent or impair our ability to maintain our licensing arrangements on acceptable terms, we or our collaborators may be unable to successfully develop and commercialize the affected product candidates.

Some of our in-licensed intellectual property has been discovered through government funded research and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies, and compliance with such regulations may limit our exclusive rights and our ability to contract with non-U.S. manufacturers.

Certain intellectual property rights that have been in-licensed pursuant to the Duke License have been generated through the use of U.S. government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or the Patent and Trademark Law Amendment. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require the licensor to grant exclusive, partially exclusive or non-exclusive licenses to any of these inventions to a third party if it determines that (1) adequate steps have not been taken to commercialize the invention, (2) government action is necessary to meet public health or safety needs or (3) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if the licensor fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States, and the Duke License requires that we comply with this requirement. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture the products substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our owned or licensed future intellectual property is also generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation with respect to our product candidates, thereby potentially extending the term of marketing exclusivity for such product candidates, our business may be harmed.

In the United States, a patent that covers an FDA-approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. In the European Union, our product candidates may be eligible for term extensions based on similar legislation. In either jurisdiction, however, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial.

Patents and patent applications involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our patent position.

The patent positions of biopharmaceutical and biotechnology companies and other actors in our fields of business can be highly uncertain and typically involve complex scientific, legal and factual analyses. In particular, the interpretation and breadth of claims allowed in some patents covering biopharmaceutical compositions may be uncertain and difficult to determine, and are often affected materially by the facts and circumstances that pertain to the patented compositions and the related patent claims. The standards of the USPTO and its foreign counterparts are sometimes uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. U.S. patents and patent applications may also be subject to interference or derivation proceedings, and U.S. patents may be subject to reexamination proceedings, post-grant review and/or *inter partes* review in the USPTO. International patents may also be subject to opposition or comparable proceedings in the corresponding international patent office, which could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such interference, derivation, reexamination, post-grant review, *inter partes* review and opposition proceedings may be costly. Accordingly, rights under any issued patents may not provide us with sufficient protection against competitive products or processes.

Furthermore, even if not challenged, our patents and patent applications may not adequately protect our technology and any product candidates or products that we develop alone or with collaborators or prevent others from designing their products to avoid being covered by our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to product candidates or potential products is threatened, it could dissuade companies from collaborating with us to develop, and could threaten our or their ability to successfully commercialize, such product candidates. Furthermore, for U.S. applications in which any claim is entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO in order to determine who was the first to invent any of the subject matter covered by such patent claims.

In addition, changes in, or different interpretations of, patent laws in the United States and other countries may permit others to use our discoveries or to develop and commercialize our technology and product candidates or products without providing any compensation to us, or may limit the scope of patent protection that we are able to obtain. The laws of some countries do not protect intellectual property rights to the same extent as U.S. laws, and those countries may lack adequate rules and procedures for defending our intellectual property rights.

If the patent applications we hold or have in-licensed with respect to our current and future research and development programs and product candidates fail to issue, if their validity, breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our technology or any products and product candidates that we or our collaborators may develop, it could dissuade companies from collaborating with us to develop product candidates, encourage competitors to develop competing products or technologies and threaten our or our collaborators' ability to commercialize future product candidates. Any such outcome could have a material adverse effect on our business.

Third parties may assert claims against us alleging infringement of their patents and proprietary rights, or we may need to become involved in lawsuits to defend or enforce our patents, either of which could result in substantial costs or loss of productivity, delay or prevent the development and commercialization of product candidates, prohibit our use of proprietary technology or sale of potential products or put our patents and other proprietary rights at risk.

Our commercial success depends in part upon our ability to develop, manufacture, market and sell product candidates without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. Litigation relating to infringement or misappropriation of patent and other intellectual property rights in the pharmaceutical, biotechnology and agricultural biotechnology industries is common, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the USPTO and corresponding international patent offices. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, many companies in intellectual property-dependent industries, including the biotechnology, agricultural biotechnology and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. Numerous United States, EU and other internationally issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our collaborators are developing product candidates, and as the biotechnology, agricultural biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties. For example, we are aware of certain patents held by third parties relating to the modification of T cells, including the production of CAR T cells. Although conducting clinical trials and other development activities with respect to our CAR T product candidates is not considered an act of infringement in the United States, if and when any of our CAR T product candidates may be approved by the FDA, those third parties may seek to enforce their patents by filing a patent infringement lawsuit against us. As a result of any patent infringement claims, or in order to avoid any potential infringement claims, we may choose to seek, or be required to seek, a license from the third party, which may require payment of substantial royalties or fees, or require us to grant a cross-license under our intellectual property rights, similar to the cross license we granted Cellectis as part of our patent litigation settlement. These licenses may not be available on reasonable terms or at all. Even if a license can be obtained on reasonable terms, the rights may be nonexclusive, which would give our competitors access to the same intellectual property rights. If we are unable to enter into a license on acceptable terms, we or our collaborators could be prevented from commercializing one or more product candidates, or forced to modify such product candidates, or to cease some aspect of our business operations, which could harm our business significantly. We or our collaborators might also be forced to redesign or modify our technology or product candidates so that we no longer infringe the third-party intellectual property rights, which may result in significant cost or delay to us, or which redesign or modification could be impossible or technically infeasible. Even if we were ultimately to prevail, any of these events could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

Further, if a patent infringement suit is brought against us, our collaborators or our third-party service providers, our development, manufacturing or sales activities relating to the product or product candidate that is the subject of the suit may be delayed or terminated. In addition, defending such claims has in the past and may in the future cause us to incur substantial expenses and, if successful, could cause us to pay substantial damages if we are found to be infringing a third party's patent rights. These damages potentially include increased damages and attorneys' fees if we are found to have infringed such rights willfully. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. In addition, if the breadth or strength of protection provided by the patents and patent applications we own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

We have been and may in the future be subject to third-party claims and similar adversarial proceedings or litigation in other jurisdictions regarding our infringement of the patent rights of third parties. Even if such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our or our collaborators' ability to further develop or commercialize the applicable product candidate unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our technologies, compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to prohibit our use of those technologies, compositions, formulations, methods of treatment, prevention or use or other technologies, effectively blocking our or our collaborators' ability to develop and commercialize the applicable product candidate until such patent expires or is finally determined to be invalid or unenforceable or unless we or our collaborators obtain a license.

Some of our competitors may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity, adversely impact prospective customers, cause product shipment delays or prohibit us from manufacturing, marketing or otherwise commercializing our products, services and technology. Any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operation, financial condition or cash flows.

If we or one of our licensors were to initiate legal proceedings against a third party to enforce a patent covering our technology or a product candidate, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and Europe, defendant counterclaims alleging invalidity or unenforceability are common. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Third parties might allege unenforceability of our patents because during prosecution of the patent an individual connected with such prosecution withheld relevant information, or made a misleading statement. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution, but that an adverse third party may identify and submit in support of such assertions of invalidity. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or product candidates. Our patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors view these announcements in a negative light, the price of our common stock could be adversely affected. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings.

Developments in patent law could have a negative impact on our business.

From time to time, the United States Supreme Court, or the Supreme Court, other federal courts, the United States Congress, or Congress, the USPTO and similar international authorities may change the standards of patentability, and any such changes could have a negative impact on our business. For example, the America Invents Act, or the AIA, which was passed in September 2011, resulted in significant changes to the U.S. patent system. An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned from a "first-to-invent" to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we made the invention before it was made by the third party. Circumstances could prevent us from promptly filing patent applications on our inventions.

The AIA limited where a patentee may file a patent infringement suit and provided opportunities for third parties to challenge any issued patent in the USPTO. Those provisions apply to all of our U.S. patents, regardless of when issued. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. These provisions could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents.

Additionally, the Supreme Court has ruled on several patent cases in recent years either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations, and there are other open questions under patent law that courts have yet to decisively address. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of our patents and patent applications. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways and could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution, but the complexity and uncertainty of European patent laws has also increased in recent years. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business.

If we were unable to protect the confidentiality of our trade secrets and enforce our intellectual property assignment agreements, our business and competitive position would be harmed.

In addition to patent protection, because we operate in the highly technical field of development of product candidates and products using genome editing, we rely significantly on trade secret protection in order to protect our proprietary technology and processes. Trade secrets are difficult to protect. Our policy is to enter into confidentiality and intellectual property assignment agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party's relationship with us. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, we may be unsuccessful in executing such an agreement with each party who in fact conceives or develops intellectual property that we regard as our own. Our assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. In addition, these agreements may be held unenforceable and may not effectively assign intellectual property rights to us. If our trade secrets and other unpatented or unregistered proprietary information are disclosed, we are likely to lose such trade secret protection.

In addition, certain provisions in our intellectual property agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could affect the scope of our rights to the relevant intellectual property or technology, or affect financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, agreements with third parties typically restrict the ability of such third parties to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified period of time in order to secure our intellectual property rights arising from the arrangement. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and product development activities that may require us to share trade secrets under the terms of our research and development collaborations or similar agreements. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not provide adequate protection for our proprietary information. For example, our security measures may not prevent an employee or consultant with authorized access from misappropriating our trade secrets and providing them to a competitor, and the recourse we have available against such misconduct may not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. Furthermore, our proprietary information may be independently developed by others in a manner that could prevent legal recourse by us. Competitors could purchase any products we may develop and commercialize and attempt to reverse engineer and replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights or design around our protected technology. In addition, our key employees, consultants, suppliers or other individuals with access to our proprietary technology and know-how may incorporate that technology and know-how into projects and inventions developed independently or with third parties. As a result, disputes may arise regarding the ownership of the proprietary rights to such technology or know-how, and any such dispute may not be resolved in our favor. If any of our confidential or proprietary information, including our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed and such disclosure or misappropriation could have a material adverse effect on our business.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world, and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. In-licensing patents covering product candidates in all countries throughout the world may similarly be prohibitively expensive, if such opportunities are available at all. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

We generally apply for patents in those countries where we intend to make, have made, use, offer for sale or sell products and where we assess the risk of infringement to justify the cost of seeking patent protection. However, we do not seek protection in all countries where we sell products and we may not accurately predict all the countries where patent protection would ultimately be desirable. If we fail to timely file a patent application in any such country or major market, we may be precluded from doing so at a later date. Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and may export otherwise infringing products to territories where we have patent protection, but where our ability to enforce our patent rights is not as strong as in the United States. These products may compete with any products that we or our collaborators may develop, and our patents or other intellectual property rights may not be effective or sufficient to prevent such competition.

The laws of some other countries do not protect intellectual property rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. Patent protection must ultimately be sought 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 countries, and we will not have the benefit of patent protection in such countries. In addition, the legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biopharmaceuticals or biotechnologies. As a result, many companies have encountered significant difficulties in protecting and defending intellectual property rights in certain jurisdictions outside the United States. Such issues may make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many other countries, including countries in the EU, have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents and could limit our potential revenue opportunities. Accordingly, our and our licensors' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Furthermore, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, subject our patents to the risk of being invalidated or interpreted narrowly, subject our patent applications to the risk of not issuing or provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded to us, if any, may not be commercially meaningful, while the damages and other remedies we may be ordered to pay such third parties may be significant. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

We have rights, through licenses from third parties and under patents that we own, to the intellectual property to develop the product candidates we are currently developing alone or with collaborators. Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, product candidates may require specific formulations to work effectively and efficiently, and these rights may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies, or companies that 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 to develop or commercialize product candidates. These established companies may have a competitive advantage over us due to their size and greater cash resources and clinical development and commercialization capabilities. We may not be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding product candidates that we may seek to acquire.

For example, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the strategic alliance. Regardless of such right of first negotiation, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us, and the institution may license such intellectual property rights to third parties, potentially blocking our ability to pursue our development and commercialization plans.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license to us intellectual property rights that we require in order to successfully develop and commercialize potential products. We also may be unable to obtain such a license or assignment on terms that would allow us to make an appropriate return on our investment. In either event, our business and prospects for growth could suffer.

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

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

Risks Related to Our Organization, Structure and Operations

We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2019, we had 199 employees. We will need to significantly expand our organization, and our future financial performance, ability to develop and commercialize product candidates alone or with collaborators and ability to compete effectively will depend in part on our ability to effectively manage any future growth. We may have difficulty identifying, hiring and integrating new personnel. Many of the biotechnology companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles and a longer history than we do. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can identify and develop product candidates, enter into collaborative arrangements and otherwise operate our business will be limited.

Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical expansion of our operations may lead to significant costs and may divert our management and business development resources from other projects, such as the development of product candidates. If we are not able to effectively manage the expansion of our operations, it may result in weaknesses in our infrastructure, increase our expenses more than expected, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity. Our future financial performance, ability to successfully commercialize any of our product candidates and our ability to compete effectively will depend, in part, on our ability to effectively manage any future growth.

We may engage in transactions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire or in-license rights to product candidates, products or technologies or to acquire other businesses. If we do identify suitable candidates, we may not be able to enter into such transactions on favorable terms, or at all. Any such acquisitions or in-licenses may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or in-license, which may negatively impact our financial condition and restrict our operations, or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the sellers of the acquired business. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. Such transactions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or in-licenses or the effect that they might have on our operating results.

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

We are highly dependent on the research and development experience, technical skills, leadership and continued service of certain members of our management and scientific teams, including Matthew Kane, our Chief Executive Officer, Derek Jantz, our Chief Scientific Officer, Jeff Smith, our Chief Technology Officer, David Thomson, our Chief Operating Officer and Christopher Heery, our Chief Medical Officer. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time upon thirty days' written notice. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and, if we retain commercialization responsibility for any product candidate we develop alone or with collaborators, sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms or at all given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. The inability to recruit, integrate, motivate and retain additional skilled and qualified personnel, or the loss of services of certain executives, key employees, consultants or advisors, may impede the progress of our research, development and commercialization objectives and have a material adverse effect on our business.

We are subject to increased costs as a result of operating as a public company, and our management will be required to devote substantial time to maintaining compliance initiatives and corporate governance practices, including establishing and maintaining proper and effective internal control over financial reporting.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the Securities Exchange Act of 1934, as amended, or the Exchange Act, including the reporting requirements thereunder, the Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Stock Market LLC, or Nasdaq, and other applicable securities rules and regulations, including requirements related to the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs, making some activities more difficult, time consuming or costly, and increasing demand on our systems and resources. When we no longer qualify as an emerging growth company, legal, accounting and other expenses are expected to further increase.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second annual report following the completion of our IPO. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 of the Sarbanes-Oxley Act within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. We may need to hire more employees in the future or engage outside consultants to comply with these requirements, which will further increase our costs and expenses. If we fail to implement the requirements of Section 404 of the Sarbanes-Oxley Act in the required timeframe, we may be subject to sanctions or investigations by regulatory authorities, including the SEC and Nasdaq. Furthermore, if we are unable to conclude that our internal control over financial reporting is effective, our investors may 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 regulatory authorities. Failure to implement or maintain an effective internal control system could also restrict our future access to the capital markets.

Our business and operations would suffer in the event of system failures or security breaches.

Despite the implementation of security measures, our computer systems, as well as those of third parties with which we have relationships, are vulnerable to damage from computer viruses, unauthorized access, natural and manmade disasters, terrorism, war and telecommunication and electrical failures. While we do not believe that we have experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our or their operations, it could result in delays and/or material disruptions of our research and development programs. For example, the loss of trial data from completed, ongoing or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability and the development of our product candidates could be delayed.

The U.S. federal and various state and foreign governments have enacted or proposed requirements regarding the collection, distribution, use, security and storage of personally identifiable information and other data relating to individuals, and U.S. federal and state consumer protection laws are being applied to enforce regulations related to the online collection, use and dissemination of data. In the ordinary course of our business, we and third parties with which we have relationships will continue to collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial subjects and employees, in data centers and on networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our and our collaborators' security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors, breaches due to employee error, technical vulnerabilities, malfeasance or other disruptions. A number of proposed and enacted federal, state and international laws and regulations obligate companies to notify individuals of security breaches involving particular personally identifiable information, which could result from breaches experienced by us or by third parties, including collaborators, vendors, contractors or other organizations with which we have formed strategic relationships. Although, to our knowledge, neither we nor any such third parties have experienced any material security breach, and even though we may have contractual protections with such third parties, any such breach could compromise our or their networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure, notifications, follow-up actions related to such a security breach or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information and significant costs, including regulatory penalties, fines and legal expenses, and such an event could disrupt our operations, cause us to incur remediation costs, damage our reputation and cause a loss of confidence in us and our or such third parties' ability to conduct clinical trials, which could adversely affect our reputation and delay our research and development programs.

We or third parties with whom we have relationships may be adversely affected by natural or manmade disasters, public health emergencies and other natural catastrophic events, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural or manmade disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, public health emergency, power outage or other event occurred that prevented us from using all or a significant portion of our facilities, that damaged our infrastructure or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time, and our research and development activities could be setback or delayed. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business, and such an event could disrupt our operations, cause us to incur remediation costs, damage our reputation and cause a loss of confidence in us and our or third parties' ability to conduct clinical trials, which could adversely affect our reputation and delay our research and development programs.

Additionally, in December 2019, a novel strain of coronavirus (COVID-19) was reported to have surfaced in Wuhan, China. In January 2020, the World Health Organization declared the novel coronavirus outbreak a "Public Health Emergency of International Concern" and the U.S. Department of State instructed travelers to avoid all nonessential travel to China. The coronavirus has impacted the global economy and may impact our operations, including the potential interruption of our clinical trial activities and our supply chain. For example, the coronavirus outbreak may delay enrollment in our clinical trials for PBCAR0191 and PBCAR20A due to prioritization of hospital resources toward the outbreak, and some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services, which would delay our ability to release clinical results and could impact our product candidate testing, development and timelines. Additionally, any required or elective quarantine or other condition that prevents us or the third parties upon whom we depend from using all or a significant portion of our or their offices, manufacturing and/or laboratory spaces or that delays delivery of necessary testing supplies, could adversely impact our product candidate testing, development and timelines. The extent to which the coronavirus will impact our business will depend on future developments and, given the uncertainty around the extent and timing of the potential future spread or mitigation and around the imposition or relaxation of protective measures, we cannot reasonably estimate the impact to our business at this time.

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

We do not carry insurance for all categories of risk that our business may encounter. If we obtain marketing approval for any product candidates that we or our collaborators may develop, we intend to acquire insurance coverage to include the sale of commercial products, but we may be unable to obtain such insurance on commercially reasonable terms or in adequate amounts. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and clinical trials or regulatory approvals for any of our product candidates could be suspended. We also expect that operating as a public company will make it 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 the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors, our board committees or as our executive officers.

Insurance coverage is becoming increasingly expensive, and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. We do not know if we will be able to maintain existing insurance with adequate levels of coverage, and any liability insurance coverage we acquire in the future may not be sufficient to reimburse us for any expenses or losses we may suffer. A successful liability claim or series of claims brought against us could require us to pay substantial amounts and cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the development and commercialization of any product candidates that we or our collaborators may develop.

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

Global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability, and similar deterioration in the credit and financial markets and confidence in economic conditions may occur in the future. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, or do not improve, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers or others with whom we have strategic relationships may not survive any difficult economic times, which could directly affect our ability to attain our operating goals.

As of December 31, 2019, we had cash and cash equivalents of $180.9 million. While we are not aware of any downgrades, material losses or other significant deterioration in the fair value of our cash equivalents since December 31, 2019, deterioration of the global credit and financial markets could negatively impact our current portfolio of cash equivalents or our ability to meet our financing objectives. Furthermore, our stock price may decline due in part to the volatility of the stock market and any general economic downturn.

If we or any of our contract manufacturers or other suppliers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur significant costs.

We and any of our contract manufacturers and suppliers are subject to numerous federal, state and local environmental, health and safety laws, regulations and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies (under which we currently have an aggregate of approximately $10 million in coverage) specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals for any product candidate we develop alone or with collaborators could be suspended, which could have a material adverse effect on our business and financial condition.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws, regulations and permitting requirements, and any third-party contract manufacturers and suppliers we engage will also be subject to such current and future regulations and requirements. These current or future laws, regulations and permitting requirements may impair our

research, development or production efforts. Failure to comply with these laws, regulations and permitting requirements, either by us or by any third-party contract manufacturers and suppliers we engage, also may result in substantial fines, penalties or other sanctions or business disruption.

Our business operations, including our current and future relationships with third parties, will expose us to penalties for potential misconduct or improper activity, including non-compliance with regulatory standards and requirements.

Complex laws constrain our business and the financial arrangements and relationships through which we conduct our operations, including how we may research, market, sell and distribute product candidates alone or with collaborators. We are exposed to the risk of fraud or other misconduct by our employees, consultants and collaborators and, if we or our collaborators commence clinical trials and proceed to commercialization, our principal investigators and commercial partners, as well as healthcare professionals, third-party payors, patient organizations and customers. For example, misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, false and/or misleading statements, corruption of government officials, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing, promotion, sales commission and customer incentive programs and other business arrangements. Such misconduct also could involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in preclinical studies or clinical trials, illegal misappropriation of study materials or other property, or improper interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our or our collaborators' reputations.

Ensuring that our internal operations and current and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, additional reporting requirements and oversight if subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, 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 similar penalties, such as criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly and time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent such activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with applicable 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 result in the imposition of any of the penalties discussed above and have a significant impact on our business and financial condition.

We are subject to complex tax rules relating to our business, and any audits, investigations or tax proceedings could have a material adverse effect on our business, results of operations and financial condition.

We are subject to income and non-income taxes in the United States. Income tax accounting often involves complex issues, and judgment is required in determining our provision for income taxes and other tax liabilities. In May 2018 we formed a subsidiary in Australia, in June 2019 we formed a subsidiary in the United Kingdom, and we may operate in other non-US jurisdictions in the future. We could become subject to income and non-income taxes in non-US jurisdictions as well. In addition, many jurisdictions have detailed transfer pricing rules, which require that all transactions with non-resident related parties be priced using arm's length pricing principles within the meaning of such rules. The application of withholding tax, goods and services tax, sales taxes and other non-income taxes is not always clear and we may be subject to tax audits relating to such withholding or non-income taxes. We believe that our tax positions are reasonable and our tax reserves are adequate to cover any potential liability. We are currently not subject to any tax audits. However, the Internal Revenue Service or other taxing authorities may disagree with our positions. If the Internal Revenue Service or any other tax authorities were successful in challenging our positions, we may be liable for additional tax and penalties and interest related thereto or other taxes, as applicable, in excess of any reserves established therefor, which may have a significant impact on our results and operations and future cash flow.

We may not be able to utilize all, or any, of our net operating loss carryforwards.

We have incurred substantial losses during our history, do not expect to become profitable in the near future, and we may never achieve profitability. As of December 31, 2019, we had U.S. federal, state, and foreign net operating loss carryforwards of $101.3 million, $101.7 million, and $0.4 million, respectively. Our federal net operating loss carryforwards of $19.7 million will begin to expire in 2030 while the remaining federal net operating loss carryforwards of $81.6 million carry forward indefinitely. The state net operating loss carryforwards begin to expire in 2025. In addition, we have U.S. federal and state research and development tax credits of $7.2 million and an amount less than $0.1 million as of December 31, 2019, respectively, available to offset future U.S. federal and state income taxes, which begin to expire in 2027 and 2030, respectively. At December 31, 2019 and December 31, 2018, we had federal Orphan Drug credits of $1.8 million and $0.7 million, respectively, which begin to expire in 2038. Unused losses generated in taxable years ending after December 31, 2017 will not expire and may be carried forward indefinitely, but will be deductible only to the extent of 80% of current year taxable income (computed without regard to the deduction for the net operating losses) in any given year. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law.

As of December 31, 2019, we have a valuation allowance for the full amount of our net deferred tax assets as the realization of the net deferred tax assets is not determined to be more likely than not. In addition, Sections 382 and 383 of the Code limit a corporation's ability to utilize its net operating loss carryforwards and certain other tax attributes (including research credits) to offset any future taxable income or tax if the corporation experiences a cumulative ownership change of more than 50% over any rolling three-year period. State net operating loss carryforwards (and certain other tax attributes) may be similarly limited. A Section 382 ownership change can therefore result in significantly greater tax liabilities than a corporation would incur in the absence of such a change, and any increased liabilities could adversely affect the corporation's business, results of operations, financial condition and cash flow. We have not yet determined if any prior change in the ownership of our equity or any change in such ownership in connection with our IPO, would trigger a Section 382 ownership change. It is possible that such a Section 382 ownership change has already occurred in prior periods. Furthermore, additional ownership changes may occur in the future as a result of events over which we will have little or no control, including purchases and sales of our equity by our 5% stockholders, the emergence of new 5% stockholders, additional equity offerings or redemptions of our stock or certain changes in the ownership of any of our 5% stockholders. As a result, our pre-2018 net operating loss carryforwards (and research tax credits) may expire prior to being used, and our net operating loss carryforwards and tax credits generated in 2018 and thereafter will be subject to a percentage limitation, upon an ownership change. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. As a result, even if we attain profitability, we may be unable to use all or a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows.

Risks Related to Owning Our Common Stock

The market price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

The market price of our common stock is likely to be highly volatile and may fluctuate substantially due to many factors, including:

- inconsistent trading volume levels of our common stock;
- announcements or expectations regarding debt or equity financing efforts;
- sales of common stock by us, our insiders or our other stockholders;
- actual or anticipated fluctuations in our financial condition and operating results;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- results from or delays in our studies or trials, or those of our collaborators, competitors or companies perceived to be similar to us;
- delay, failure or discontinuation of any of our product development and research programs, or those of our collaborators, competitors or companies perceived to be similar to us;
- announcements about new research programs or product candidates from us or our collaborators, our competitors or companies perceived to be similar to us;
- announcements by us, our collaborators, our competitors or companies perceived to be similar to us relating to significant acquisitions, strategic partnerships or alliances, joint ventures, collaborations or capital commitments;

- actual or anticipated changes in our growth rate relative to our competitors or companies perceived to be similar to us;
- fluctuations in the valuation of our collaborators, our competitors or companies perceived to be comparable to us;
- a lack of, limited or withdrawal of coverage by security analysts, or positive or negative recommendations by them;
- actual or expected changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- publication of research reports about us, genome editing or the biopharmaceutical and agricultural biotechnology industries;
- developments or changing views regarding the use of genomic products, including those that involve genome editing;
- our ability to effectively manage our growth;
- the recruitment or departure of key personnel;
- the results of any efforts by us to identify, develop, acquire or in-license additional product candidates, products or technologies;
- unanticipated serious safety concerns related to the use of any of our product candidates, or those of our competitors or companies perceived to be similar to us;
- the termination of a collaboration agreement, licensing agreement or other strategic arrangement or the inability to establish additional strategic arrangements on favorable terms, or at all;
- regulatory actions with respect to any of our product candidates, or those of our competitors or companies perceived to be similar to us;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- regulatory or legal developments in the United States and other countries;
- changes in physician, hospital, healthcare provider or agricultural practices that may make our or our collaborators' products less useful;
- changes in the structure of healthcare payment systems;
- significant lawsuits, such as products liability, patent or stockholder litigation; and
- general economic, industry and market conditions.

These and other market and industry factors may cause the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance. These factors may have a material adverse effect on the market price and liquidity of our common stock, which may limit or prevent you from readily selling your shares of common stock and may affect our ability to obtain financing or enter into desired strategic relationships.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

We do not currently intend to pay dividends on our common stock.

We do not intend to pay any dividends to holders of our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. In addition, pursuant to our loan and security agreement with PWB we are prohibited from

paying cash dividends without the prior written consent of PWB and future debt instruments may materially restrict our ability to pay dividends on our common stock. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future, and the success of an investment in our common stock will depend upon any future appreciation in its value. Consequently, you may need to sell all or part of your common stock after price appreciation, which may never occur, as the only way to realize any future gains on your investment.

If securities or industry analysts issue an adverse or misleading opinion regarding our common stock, our stock price and trading volume could decline.

The trading market for our common stock relies in part on the research and reports that industry or securities analysts publish about us or our business. We do not control these analysts. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies and clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Provisions in our amended and restated certificate of incorporation and restated bylaws or Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and therefore depress the trading price of our common stock.

Provisions in our amended and restated certificate of incorporation and our restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. 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 our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing:

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

Moreover, because we are incorporated in 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.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum 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, officers or employees.

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum to the fullest extent permitted by law, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim for breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware, our amended and restated certificate of incorporation or our amended and restated bylaws, (4) any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws, or (5) any action asserting a claim governed by the internal affairs doctrine. Under our amended and restated certificate of incorporation, this exclusive forum provision will not apply to claims which are vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery of the State of Delaware, or for which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. For instance, the provision would not apply to actions arising under federal securities laws, including suits brought to enforce any liability or duty created by the Exchange Act or the rules and regulations thereunder. 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, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. For example, stockholders who do bring a claim in the Court of Chancery could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near the State of Delaware. The Court of Chancery may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders.

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

We are an "emerging growth company," as defined in the JOBS Act. We will remain an emerging growth company until the earlier of (1) December 31, 2024, (2) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more, (3) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years, or (4) the date on which we are deemed to be a large accelerated filer under the rules of the SEC which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to present only two years of "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this Annual Report on Form 10-K;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- 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 in this Annual Report on Form 10-K and our periodic reports, proxy statements and registration statements; 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.

We have taken advantage of reduced reporting burdens in this Annual Report on Form 10-K. In particular, we have provided only two years of "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure, and we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. 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 these accounting standards until they would otherwise apply to private companies. We have elected to take advantage of this extended transition period.

We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than $100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors.

We may choose to take advantage of some, but not all, of the available exemptions for emerging growth companies and smaller reporting companies. 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 reduced or more volatile.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We currently occupy approximately 68,000 square feet of office and laboratory space at our corporate headquarters in Durham, North Carolina under a lease that expires in 2024. We also occupy approximately 15,500 square feet of laboratory and office space used by our wholly owned subsidiary, Elo Life Systems, in Durham, North Carolina under a lease that expires in 2026, and we occupy approximately 33,600 square feet of manufacturing, laboratory and office space used for our Manufacturing Center for Advanced Technologies in Research Triangle Park, North Carolina under a lease that expires in 2027.

Item 3. Legal Proceedings.

We are not currently party to any material legal proceedings.

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.

On March 27, 2019, our common stock began trading on The Nasdaq Global Select Market under the symbol "DTIL." Prior to that time, there was no public market for our common stock.

Holders of Common Stock

As of March 2, 2020, there were approximately 221 holders of record of our common stock. This number does not include "street name" or beneficial holders, whose shares are held of record by banks, brokers, financial institutions and other nominees.

Dividend Policy

We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. In addition, pursuant to our loan and security agreement with Pacific Western Bank ("PWB"), we are prohibited from paying cash dividends without the prior written consent of PWB and future debt instruments may materially restrict our ability to pay dividends on our common stock. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors our board of directors deems relevant, and subject to any restrictions applicable to us contained in any future financing instruments.

Item 6. Selected Financial Data.

The following table sets forth our selected consolidated financial data. We derived the consolidated statement of operations data for the years ended December 31, 2019 and December 31, 2018 and the consolidated balance sheet data as of December 31, 2019 and December 31, 2018, from our audited consolidated financial statements, included elsewhere in this Annual Report on Form 10-K. We have derived the consolidated statement of operations data for the year ended December 31, 2017 from our audited consolidated financial statements not included in this report. The selected financial data should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Item 7 of Part II to this Annual Report on Form 10-K and our consolidated financial statements and the related notes thereto, included elsewhere in this Annual Report on Form 10-K. Our historical results are not necessarily indicative of our future results.

	For the Years Ended December 31,		
(in thousands, except share and per share data)	**2019**	**2018**	**2017**
Consolidated Statements of Operations Data:			
Revenue	$ 22,238	$ 10,883	$ 6,484
Operating expenses			
Research and development	82,416	45,122	20,324
General and administrative	27,026	13,673	8,016
Impairment of intangible assets	—	—	118
Total operating expenses	109,442	58,795	28,458
Loss from operations	(87,204)	(47,912)	(21,974)
Other income (expense), net:			
Change in fair value of convertible note payable	(9,758)	—	—
Interest expense	(182)	—	—
Interest income	4,267	1,875	872
Total other income (expense), net	(5,673)	1,875	872
Net loss and net loss attributable to common stockholders	$ (92,877)	$ (46,037)	$ (21,102)
Net loss per share attributable to common stockholders-basic and diluted	$ (2.21)	$ (2.92)	$ (1.33)
Weighted average shares of common stock outstanding-basic and diluted	41,991,162	15,775,541	15,906,793

(in thousands)	Years ended December 31, 2019	2018	2017
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 180,886	$ 103,193	$ 62,802
Total assets	235,233	138,600	72,682
Total current liabilities	26,932	14,075	9,203
Total noncurrent liabilities	69,987	84,565	89,848
Total stockholders' equity (deficit)	138,314	39,960	(26,369)
Total liabilities and stockholders' equity (deficit)	$ 235,233	$ 138,600	$ 72,682

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

You should read the following discussion and analysis of financial condition and operating results together with the section captioned "Selected Consolidated Financial Data" and our consolidated financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. As a result of many factors, such as those set forth in the section of the Annual Report on Form 10-K captioned "Risk Factors" and elsewhere in this Annual Report on Form 10-K, our actual results may differ materially from those anticipated in these forward-looking statements.

Overview

We are a life sciences company dedicated to improving life through the application of our pioneering, proprietary ARCUS genome editing platform. We leverage ARCUS in the development of our product candidates, which are designed to treat human diseases and create healthy and sustainable food and agricultural solutions. We are actively developing product candidates in three innovative areas: allogeneic CAR T cell immunotherapy, *in vivo* gene correction, and food. We are currently conducting a Phase 1/2a clinical trial of PBCAR0191 in adult patients with relapsed or refractory, or R/R, non-Hodgkin lymphoma, or NHL, or R/R B-cell precursor acute lymphoblastic leukemia, or B-ALL. PBCAR0191 is our first gene-edited allogeneic chimeric antigen receptor, or CAR, T cell therapy candidate targeting CD19 and is being developed in collaboration with Les Laboratoires Servier, or Servier. We have received orphan drug designation for PBCAR0191 from the U.S. Food and Drug Administration, or FDA, for the treatment of ALL. Made from donor-derived T cells modified using our ARCUS genome editing technology, PBCAR0191 recognizes the well characterized tumor cell surface protein CD19, an important and validated target in several B-cell cancers, and is designed to avoid graft-versus-host disease, or GvHD, a significant complication associated with donor-derived, cell-based therapies. We believe that this trial, which is designed to assess the safety and tolerability of PBCAR0191 at increasing dose levels, as well as to evaluate anti-tumor activity, is the first U.S.-based clinical trial to evaluate an allogeneic CAR T therapy for R/R NHL. Furthermore, we believe that our proprietary, one-step engineering process for producing allogeneic CAR T cells with a potentially optimized cell phenotype, at large scale in a cost-effective manner, will enable us to overcome the fundamental clinical and manufacturing challenges that have limited the CAR T field to date.

In December 2019, we announced initial data from this ongoing Phase 1/2a clinical trial of PBCAR0191 in adult patients with R/R NHL and R/R B-ALL. A total of nine adult patients were reported in these initial Phase 1 trial results, including six with NHL (three treated at Dose Level 1 ($3x10^5$ cells/kg), or DL1, and three treated at Dose Level 2 ($1x10^6$ cells/kg), or DL2), and three with B-ALL (all treated at DL2). These data indicated no serious adverse events or dose limiting toxicities. In the NHL cohort, four of six patients demonstrated an objective tumor response by Lugano criteria at day 28, for an overall objective response rate of 67%, including three partial responses and one complete response. In the ALL cohort, one of three patients achieved a complete response at day 28 following treatment with PBCAR0191. As of December 31, 2019, dosing of patients at Dose Level 3 ($3x10^6$ cells/kg) was underway. Based on the data observed at DL1 and DL2, we filed a protocol amendment for this trial with the FDA in December 2019. The amended trial design is intended to specifically address key clinical questions. These include assessing the impact of higher total doses of cells on clinical activity and/or the impact of modified lymphodepletion on the ability to achieve durable clinical benefit with associated CAR T cell expansion and persistence. Following feedback from the FDA in late January 2020, the protocol amendment is now being implemented.

In September 2019, the FDA accepted our investigational new drug, or IND, application for our second allogeneic CAR T cell therapy product candidate, PBCAR20A, for which we expect to commence a Phase 1/2a clinical trial in the first quarter of 2020. PBCAR20A is wholly owned by us and targets the validated tumor cell surface target CD20. It will be investigated in subjects with NHL, chronic lymphocytic leukemia, or CLL, and small lymphocytic lymphoma, or SLL. A subset of the NHL patients will have the diagnosis of mantle cell lymphoma, or MCL, and we have received orphan drug designation for PBCAR20A from the FDA for the treatment of this disease. Based on the adverse events observed to date with PBCAR0191, the FDA has agreed to allow us to commence dosing with PBCAR20A directly at Dose Level 2, which we expect to accelerate the timing for our expected completion of the trial.

In January 2020, the FDA accepted our IND application for our third allogeneic CAR T cell therapy product candidate, PBCAR269A, for which we expect to commence a Phase 1/2a clinical trial in 2020. PBCAR269A is wholly owned by us and is designed to target the validated tumor cell surface target BCMA. It will be investigated in subjects with R/R multiple myeloma and we have received orphan drug designation from the FDA for this indication.

Also in January 2020, we announced that we expect to advance a program targeting the rare genetic disease primary hyperoxaluria type 1, or PH1 as our lead wholly owned *in vivo* gene correction program. PH1 affects approximately 1-3 people per million in the United States and is caused by loss of function mutations in the AGXT gene, leading to the accumulation of calcium oxalate crystals in the kidneys. Patients suffer from painful kidney stones which may ultimately lead to renal failure. Using ARCUS, we are developing a potential therapeutic approach to the treatment of PH1 that involves knocking out a gene called HAO1 which acts upstream of AGXT. Suppressing HAO1 has been shown in preclinical models by us to prevent the formation of calcium oxalate. We therefore believe that a one-time administration of an ARCUS nuclease targeting HAO1 may be a viable strategy for a durable treatment of PH1 patients. In preclinical studies we have demonstrated in a mouse model of PH1 that administration of an ARCUS nuclease targeting HAO1 resulted in approximately 70% reduction in urine calcium oxalate levels. We have also demonstrated that ARCUS efficiently knocked out the HAO1 gene in non-human primates. We plan to select a clinical candidate for this program during 2020.

During the fiscal year ended December 31, 2019, we opened our Manufacturing Center for Advanced Therapeutics, or MCAT, which we believe is the first in-house current good manufacturing practice, or cGMP, compliant manufacturing facility dedicated to genome-edited, off-the-shelf CAR T cell therapy product candidates in the United States. MCAT will enable in-house production of three different drug substances: allogeneic CAR T cells, messenger RNA (including formulations development) and adeno-associated viral vectors. We are currently using this new manufacturing center to create clinical trial material to be used in our BCMA targeting allogeneic CAR T clinical trials beginning in 2020. We believe MCAT confers a number of strategic advantages including cost benefits, control of our manufacturing process and strategic flexibility as we execute our clinical trials. In the longer term, we believe MCAT has the potential to be a commercial launch facility.

Since our formation in 2006, we have devoted substantially all of our resources to developing ARCUS, conducting research and development activities, recruiting skilled personnel, developing manufacturing processes, establishing our intellectual property portfolio and providing general and administrative support for these operations. We have financed our operations primarily with proceeds from our IPO, the sale of our convertible preferred stock and upfront payments from licensing arrangements.

On April 1, 2019, we completed our IPO of 9,085,000 shares of common stock, including the underwriters' full exercise of their option to purchase an additional 1,185,000 additional shares of common stock, at an offering price of $16.00 per share, for net proceeds of approximately $130.5 million after deducting underwriting discounts and commissions and offering expenses payable by us. To date, we have generated approximately $475.4 million from third parties through a combination of financings including through our IPO, preferred stock and convertible note financings, an upfront payment under the Servier Agreement and additional funding from other strategic alliances and grants.

Since our inception, we have incurred significant operating losses and have not generated any revenue from the sale of products. Our ability to generate any product revenue or product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more of our product candidates or the product candidates of our collaborators for which we may receive milestone payments or royalties. Our net losses were $92.9 million and $46.0 million for the years ended December 31, 2019 and December 31, 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $177.1 million.

We expect our operating expenses to increase substantially in connection with the expansion of our product development programs and capabilities. We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for one of our product candidates or the product candidates of our collaborators for which we may receive milestone payments or royalties. If we obtain regulatory approval for any of our product candidates, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing and distribution. In addition, we expect to continue to incur additional costs associated with operating as a public company.

As a result of these anticipated expenditures, we will need additional financing to support our continuing operations. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our cash needs through a combination of public equity, debt financings or other sources, which may include current and new collaborations with third parties. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We cannot assure you that we will ever generate significant revenue to achieve profitability.

Because of the numerous risks and uncertainties associated with the development of therapeutic and agricultural products, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be required to raise additional capital on terms that are unfavorable to us or we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

We currently conduct our operations through two reportable segments: Therapeutics and Food. Our Therapeutics segment is focused on allogeneic CAR T immunotherapy and *in vivo* gene correction. Our Food segment focuses on applying ARCUS to develop food and nutrition products through collaboration agreements with consumer-facing companies.

Collaborations

Gilead

In September 2018, we and Gilead entered into a collaboration and license agreement, which we refer to as the Gilead Agreement, to develop genome editing tools using ARCUS to target viral DNA associated with the Hepatitis B virus. Pursuant to the terms of the agreement, Gilead received an exclusive license to exploit the resulting synthetic nucleases and products that use them to treat the Hepatitis B virus in humans, and we are entitled to receive up to approximately $40.0 million in research funding over an initial three year term and milestone payments of up to an aggregate of $445.0 million, consisting of up to $105.0 million in development milestone payments and up to $340.0 million in commercial milestone payments. We are also entitled to receive tiered royalties ranging from the high single digit percentages to the mid-teen percentages on worldwide net sales of the products developed through the term of the agreement, subject to customary potential reductions.

We recognized $13.3 million and $3.7 million in revenues under the Gilead Agreement during the years ended December 31, 2019 and December 31, 2018, respectively, and recorded $1.5 million and $2.3 million in deferred revenue as of December 31, 2019 and December 31, 2018, respectively. We did not receive any milestone payments under the Gilead Agreement during the years ended December 31, 2019 or December 31, 2018.

Servier

In February 2016, we entered into the Servier Agreement, pursuant to which we have agreed to develop allogeneic CAR T cell therapies for up to six unique antigen targets. One target was selected at the agreement's inception. Upon selection of an antigen target under the agreement, we have agreed to perform early-stage research and development on individual T cell modifications for the selected target, develop the resulting therapeutic product candidates through Phase 1 clinical trials and prepare clinical trial material of such product candidates for use in Phase 2 clinical trials.

We received an upfront payment of $105.0 million under the Servier Agreement. We have the ability to receive total payments, including the upfront payment, option fees and milestone payments, in the aggregate across all six targets, of up to approximately $1.6 billion. This includes up to $1.5 billion in milestone payments, consisting of up to $401.3 million in development milestone payments and up to $1.1 billion in commercial milestone payments. We are also entitled to receive tiered royalties ranging from the mid-single digit percentages to the sub-teen percentages on worldwide net sales, subject to potential customary reductions. We also have the right to participate in the development and commercialization of any licensed products resulting from the collaboration through a 50/50 co-development and co-promotion option in the United States, subject to our payment of an option fee, which is exercisable after Servier's commercial option exercise.

Under the Servier Agreement, we recognized $7.3 million and $5.8 million in revenues during the years ended December 31, 2019 and December 31, 2018, respectively. The amount recorded as deferred revenue was $80.9 million and $88.6 million as of December 31, 2019 and December 31, 2018, respectively. No development or sales-based milestones were received for the fiscal years ended December 31, 2019 or December 31, 2018.

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales in the foreseeable future. We record revenue from collaboration agreements, including amounts related to upfront payments, annual fees for licenses of our intellectual property and research and development funding.

Research and Development Expenses

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

- salaries, benefits and other related costs, including share-based compensation expense, for personnel engaged in research and development functions;
- expenses incurred under agreements with third parties, including contract research organizations, or CROs, and other third parties that conduct preclinical research and development activities and clinical trials on our behalf;
- costs of developing and scaling our manufacturing process and manufacturing drug products for use in our preclinical studies and ongoing and future clinical trials, including the costs of contract manufacturing organizations, or CMOs, and our MCAT facility that will manufacture our clinical trial material for use in our preclinical studies and ongoing and potential future clinical trials;
- costs of outside consultants, including their fees and related travel expenses;
- costs of laboratory supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials;

- license payments made for intellectual property used in research and development activities; and

- facility-related expenses, which include direct depreciation costs and expenses for rent and maintenance of facilities and other operating costs if specifically identifiable to research activities.

We expense research and development costs as incurred. We track external research and development costs, including the costs of laboratory supplies and services, outsourced research and development, clinical trials, contract manufacturing, laboratory equipment and maintenance and certain other development costs, by product candidate when the program IND application is accepted by the FDA. Internal and external costs associated with infrastructure resources, other research and development costs, facility related costs and depreciation and amortization that are not identifiable to a specific product candidate are included in the platform development, early-stage research and unallocated expenses category in the table below.

The following table summarizes our research and development expenses by product candidate or development program for the periods presented:

(in thousands)	Years ended December 31, 2019	2018	Change
Direct research and development expenses by product candidate:			
CD19 external development costs	$ 4,726	$ 13,654	$ (8,928)
CD20 external development costs	9,375	—	9,375
BCMA external development costs	4,928	—	4,928
Platform development, early-stage research and unallocated expenses:			
Employee-related costs	26,383	14,784	11,599
Laboratory supplies and services	11,706	4,061	7,645
Outsourced research and development	12,416	7,055	5,361
CMOs and research organizations	1,770	—	1,770
Laboratory equipment and maintenance	1,381	519	862
Facility-related costs	3,030	1,431	1,599
Depreciation and amortization	4,186	1,759	2,427
Licensing fees	2,236	643	1,593
Other research and development costs	279	1,216	(937)
Total research and development expenses	$ 82,416	$ 45,122	$ 37,294

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase substantially for the foreseeable future and will comprise a larger percentage of our total expenses as we continue our Phase 1/2a clinical trial for our CD19 product candidate, commence a Phase 1/2a clinical trial for our CD20 product candidate, commence a Phase 1/2a clinical trial for our BCMA product candidate, and continue to discover and develop additional product candidates.

We cannot determine with certainty the duration and costs of ongoing and future clinical trials of our CD19, CD20, and BCMA product candidates, or any other product candidate we may develop or if, when or to what extent we will generate revenue from the commercialization and sale of any product candidate for which we obtain marketing approval. We may never succeed in obtaining marketing approval for any product candidate. The duration, costs and timing of clinical trials and development of our CD19, CD20, and BCMA product candidates, and any other our product candidate we may develop will depend on a variety of factors, including:

- the scope, rate of progress, expense and results of clinical trials of our CD19, CD20, and BCMA product candidates, as well as of any future clinical trials of other product candidates and other research and development activities that we may conduct;

- uncertainties in clinical trial design and patient enrollment rates;

- the actual probability of success for our product candidates, including their safety and efficacy, early clinical data, competition, manufacturing capability and commercial viability;

- significant and changing government regulation and regulatory guidance;

- the timing and receipt of any marketing approvals; and

- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in our clinical trials due to slower than expected patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including share-based compensation, for personnel in our executive, finance, business development, operations and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and expenses for rent and maintenance of facilities and other operating costs that are not specifically attributable to research activities.

We expect that our general and administrative expenses will increase in the future as we increase our personnel headcount to support our continued research activities and development of product candidates. We also expect to incur increased expenses associated with being a public company, including costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with Nasdaq and SEC requirements; director and officer insurance costs; and investor and public relations costs.

Change in Fair Value of Convertible Notes Payable

We elected on issuance to account for the convertible notes payable we issued in March 2019, or the 2019 Notes, at fair value until their settlement. The change in fair value of the 2019 Notes was recognized through the statement of operations. The 2019 Notes settled into 2,921,461 shares of common stock on the closing of our IPO on April 1, 2019.

Interest Expense

Interest expense consists of interest from the 2019 Notes at a rate of 6% per annum.

Interest Income

Interest income consists of interest income earned on our cash and cash equivalents.

Income Taxes

Since our inception in 2006, we have generated cumulative federal and state net operating loss and R&D credit carryforwards for which we have not recorded any net tax benefit due to the uncertainty around utilizing these tax attributes within their respective carryforward periods. As of December 31, 2019, we had federal, state, and foreign net operating loss carryforwards of $101.3 million, $101.7 million, and $0.4 million, respectively, which may be available to offset future taxable income. The U.S. federal net operating loss carryforwards of $19.7 million will begin to expire in 2030 while the remaining federal net operating loss carryforwards of $81.6 million carry forward indefinitely. The state net operating loss carryforwards begin to expire in 2025. As of December 31, 2019, we also had federal research and development tax credit carryforwards of $7.2 million, which begin to expire in 2027. As of December 31, 2019 and December 31, 2018, we had federal Orphan Drug credits of $1.8 million and $0.7 million, respectively, which begin to expire in 2038. As of December 31, 2019, we also have federal contribution carryforwards of $0.1 million, which begin to expire in 2020. We have recorded a full valuation allowance against our net deferred tax assets at each balance sheet date.

On December 22, 2017, the TCJA was signed into United States law. The TCJA includes a number of changes to existing tax law, including, among other things, a permanent reduction in the federal corporate income tax rate from a top marginal tax rate of 35% to a flat rate of 21%, effective as of January 1, 2018, as well as a limitation of the deduction for net operating losses to 80% of annual taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely). The federal tax rate change resulted in a reduction in the gross amount of our deferred tax assets and liabilities recorded as of December 31, 2017, and a corresponding reduction in our valuation allowance. As a result, no income tax expense or benefit was recognized as of the enactment date of the TCJA.

Results of Operations

Comparison of the Years Ended December 31, 2019 and December 31, 2018

The following table summarizes our results of operations for the years ended December 31, 2019 and December 31, 2018, together with the changes in those items in dollars:

(in thousands)	Years ended December 31, 2019	2018	Change
Revenue	$ 22,238	$ 10,883	$ 11,355
Operating expenses:			
Research and development	82,416	45,122	37,294
General and administrative	27,026	13,673	13,353
Total operating expenses	109,442	58,795	50,647
Loss from operations	(87,204)	(47,912)	(39,292)
Other income (expense), net:			
Change in fair value of convertible note payable	(9,758)	—	(9,758)
Interest expense	(182)	—	(182)
Interest income	4,267	1,875	2,392
Total other income (expense), net	(5,673)	1,875	(7,548)
Net loss	$ (92,877)	$ (46,037)	$ (46,840)

Revenue

Revenue for the year ended December 31, 2019 was $22.2 million, compared to $10.9 million for the year ended December 31, 2018. The increase of $11.3 million in revenue during the year ended December 31, 2019 was primarily the result of a $9.6 million increase in research revenue recognized from Gilead as 2019 was the first full year of revenue recognized under the Gilead agreement initiated in September 2018 and a $1.5 million increase in collaboration revenue recognized from Servier.

Research and Development Expenses

(in thousands)	Years ended December 31, 2019	2018	Change
Direct research and development expenses by product candidate:			
CD19 external development costs	$ 4,726	$ 13,654	$ (8,928)
CD20 external development costs	9,375	—	9,375
BCMA external development costs	4,928	—	4,928
Platform development, early-stage research and unallocated expenses:			
Employee-related costs	26,383	14,784	11,599
Laboratory supplies and services	11,706	4,061	7,645
Outsourced research and development	12,416	7,055	5,361
CMOs and research organizations	1,770	—	1,770
Laboratory equipment and maintenance	1,381	519	862
Facility-related costs	3,030	1,431	1,599
Depreciation and amortization	4,186	1,759	2,427
Licensing fees	2,236	643	1,593
Other research and development costs	279	1,216	(937)
Total research and development expenses	$ 82,416	$ 45,122	$ 37,294

Research and development expenses for the year ended December 31, 2019 were $82.4 million, compared to $45.1 million for the year ended December 31, 2018. The increase of $37.3 million was primarily due to a $31.9 million increase in platform development, early-stage research and unallocated expenses, a $9.4 million and $4.9 million increase in direct research and development expenses related to our CD20 and BCMA programs, respectively, partially offset by a decrease in direct research and development expenses related to our CD19 program of $8.9 million.

The increase in direct research and development expenses for our CD20 and BCMA programs was due to increases in lab services and CMO and research organization costs as we prepare to enter planned Phase 1/2a clinical trials in 2020. This was partially offset by a decrease in our CD19 expenses primarily due to lower spending on CMO and research organization costs.

Platform development, early-stage research and unallocated expenses increased primarily due to a $11.6 million increase in employee-related costs associated with increased headcount to support our technology platform development and manufacturing capabilities, a $7.6 million increase in laboratory supplies and services, a $5.4 million increase in outsourced research and development spending and $2.4 million increase in depreciation and amortization in the year ended December 31, 2019 compared to the year ended December 31, 2018.

General and Administrative Expenses

General and administrative expenses were $27.0 million for the year ended December 31, 2019 compared to $13.7 million for the year ended December 31, 2018. The increase of $13.3 million was primarily due to an increase of $6.2 million in employee-related costs as we increased our general and administrative headcount, $2.7 million in consulting fees, $2.1 million in increased administrative costs, including insurance, franchise and property taxes, bank fees, and costs related to operating as a public company, and $1.4 million in facility related costs.

Change in Fair Value of Convertible Notes Payable

We elected on issuance to account for the 2019 Notes at fair value until their settlement. For the year ended December 31, 2019, we recognized $9.8 million of expense as changes in fair value. The 2019 Notes were settled on the closing of the IPO in April 2019.

Interest Expense

Interest expense of $0.2 million for the year ended December 31, 2019 consists of interest from the 2019 Notes at a rate of 6% per annum.

Interest Income

Interest income was $4.3 million for the year ended December 31, 2019 compared to $1.9 million for the year ended December 31, 2018. The increase of $2.4 million of interest income generated on our cash and cash equivalent balances was the result of lower interest rates and having higher cash balances invested in the year ended December 31, 2019 compared to the year ended December 31, 2018.

Segment Results

The following tables summarize segment revenues and segment operating loss (see Note 13 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding our segments):

	For the Years Ended December 31,	
(in thousands)	**2019**	**2018**
Revenue:		
Therapeutics	$ 20,632	$ 9,523
Food	1,606	1,360
Total segment revenue	22,238	10,883
Segment operational cash expenditures:		
Therapeutics	$ 45,941	$ 35,045
Food	6,984	9,125
Total segment operational cash expenditures	52,925	44,170
Allocation of centralized research and development operational cash expenditures:		
Therapeutics	$ 24,118	$ 11,605
Food	—	2,901
Total allocation of centralized research and development operational cash expenditures	24,118	14,506
Segment operating income (loss):		
Therapeutics	$ (49,427)	$ (37,127)
Food	(5,378)	(10,666)
Total segment operating loss	$ (54,805)	$ (47,793)

We evaluate the operating performance of each segment based on segment operating loss. Segment operating loss is derived by deducting operational cash expenditures, net, from GAAP revenue. Operational cash expenditures are cash disbursements made that are specifically identifiable to the reportable segment (including specifically identifiable research and development and property, equipment and software expenditures). For the year ended December 31, 2018, we allocated centralized research and development expenditures for early stage research, nuclease development and the purchase of general laboratory supplies to the Therapeutics and Food segments based on headcount. In January 2019, the Food segment moved into a new leased facility in Durham, North Carolina. We have determined that the Food segment is no longer deriving benefit from the Company's centralized research and development expenditures, thus all these expenditures were allocated to the Therapeutics segment for the year ended December 31, 2019. The reportable segment and centralized research and development operational cash expenditures include cash disbursements for compensation, laboratory supplies, purchases of property, equipment and software and procuring services from CROs, CMOs and research organizations. We do not allocate general operational expenses or non-cash income statement amounts to our reportable segments.

Therapeutics Segment

Revenue for the year ended December 31, 2019 was $20.6 million, compared to $9.5 million for the year ended December 31, 2018. The increase of $11.1 million was primarily the result of a $9.6 million increase in research funding from Gilead and $1.5 million increase in revenue from Servier. Segment operational cash expenditures for the year ended December 31, 2019 were $45.9 million, compared to $35.0 million for the year ended December 31, 2018. The increase of $10.9 million in operational cash expenditures was primarily due to an increase in payments made to service providers for contract manufacturing and clinical trial research, laboratory supplies and services, employee headcount and fixed assets for the build out of our manufacturing capabilities, offset by a decrease in payments made to the University of Pennsylvania, which is early stage research and not considered specific to any one therapeutic area. As a result, these payments were classified as centralized research and development expenditures in the year ended December 31, 2019 as opposed to being classified as Therapeutics operational cash expenditures in the year ended December 31, 2018. Segment operating loss increased $12.3 million from $37.1 million for the year ended December 31, 2018 to $49.4 million for the year ended December 31, 2019 primarily due to the factors discussed above.

Food Segment

Revenue for the year ended December 31, 2019 was $1.6 million, compared to $1.4 million for the year ended December 31, 2018. The increase of $0.2 million was primarily attributable to $0.4 million from a new customer agreement with a collaboration partner entered into during the year ended December 31, 2019 offset by a $0.2 million decrease in revenue from a collaboration partner. Segment operational cash expenditures for the year ended December 31, 2019 were $7.0 million, compared to $9.1 million for the year ended December 31, 2018. The decrease of $2.1 million was primarily due to a decrease in leasehold improvements, which is attributable to large construction expenditures made in the year ended December 31, 2018 for work done to our leased facility that did not occur in the year ended December 31, 2019, as our Food segment moved into the facility in January 2019. This decrease in spending was offset by increases in laboratory equipment, furniture and fixtures, laboratory supplies, employee headcount and rent. Segment operating loss decreased $5.3 million from $10.7 million for the year ended December 31, 2018 to $5.4 million for the year ended December 31, 2019 primarily due to the factors discussed above.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the preclinical and clinical development of our product candidates. We expect that our research and development and general and administrative costs will continue to increase, including in connection with conducting preclinical studies and clinical trials for our product candidates, contracting with CROs and CMOs, the addition of laboratory equipment to MCAT in support of preclinical studies and clinical trials, expanding our intellectual property portfolio and providing general and administrative support for our operations. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements or other sources. We do not currently have any approved products and have never generated any revenue from product sales.

We have financed our operations primarily with proceeds from our IPO, the sale of our convertible preferred stock and upfront payments from collaboration and licensing arrangements. On April 1, 2019, we completed our IPO of 9,085,000 shares of common stock, including the underwriters' full exercise of their option to purchase an additional 1,185,000 additional shares of common stock, at an offering price of $16.00 per share, for net proceeds of approximately $130.5 million after deducting underwriting discounts and commissions and offering expenses payable by us. To date, we have generated approximately $475.4 million from third parties through a combination of financings including through our IPO, preferred stock and convertible note financings, an upfront payment under the Servier Agreement and additional funding from other strategic alliances and grants.

In May 2019, we entered into a loan and security agreement (the "Pacific Western Loan Agreement") with PWB pursuant to which we may request advances on a revolving line of credit of up to an aggregate principal of $50.0 million (the "Revolving Line"). The Pacific Western Loan Agreement was amended (the "PWB Amendment") in December 2019 to allow the Company to maintain a bank account with a non-affiliated bank in the United Kingdom provided that the account balance does not exceed 1.5 million GBP or its U.S. dollar equivalent at any time. As of December 31, 2019, we had no borrowings under our Revolving Line and were in compliance with its financial covenants.

Cash Flows

Our cash and cash equivalents totaled $180.9 million as of December 31, 2019, compared to $103.2 million as of December 31, 2018. As of December 31, 2019, we had no borrowings under our revolving line of credit.

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

	For the Years Ended December 31,	
(in thousands)	**2019**	**2018**
Net cash used in operating activities	$ (71,015)	$ (51,723)
Net cash used in investing activities	(24,666)	(15,663)
Net cash provided by financing activities	173,374	107,777
Increase in cash and cash equivalents	$ 77,693	$ 40,391

Cash Flows for the Year ended December 31, 2019

Operating Activities

Net cash used in operating activities for the year ended December 31, 2019 was $71.0 million, driven primarily by our net loss of $92.9 million as we incurred expenses associated with our CD19, CD20, and BCMA programs, platform development and early-stage research, and general and administrative expenses, and a decrease in operating assets and liabilities of $2.4 million, partially offset by net non-cash expenses of $24.2 million.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2019 was $24.7 million, which was attributable to purchases of property, equipment and software.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2019 was $173.4 million, consisting of $130.5 million in proceeds from our IPO, net of issuance costs, the net proceeds from the issuance of our 2019 Notes of $39.6 million, and $1.3 million in proceeds from stock option exercises.

Debt Obligations

In March 2019, we issued an aggregate principal amount of $39.6 million of 2019 Notes in a private placement transaction. Upon settlement, the change in fair value of the 2019 Notes was $9.8 million and the accrued interest on the 2019 Notes was $0.2 million. Pursuant to their terms, the 2019 Notes were settled in 2,921,461 shares of our common stock upon the closing of our IPO at a settlement price of $13.60 per share, which is equal to 85% of the IPO price per share.

In May 2019, we entered into a loan and security agreement with Pacific Western Bank pursuant to which we may request advances on a $50.0 million revolving line of credit.

Cash Flows for the Year Ended December 31, 2018

Operating Activities

Net cash used in operating activities for the year ended December 31, 2018 was $51.7 million, primarily consisting of our net loss of $46.0 million as we incurred expenses associated with our CD19 program, platform development and early-stage research and general and administrative expenses. In addition, we had non-cash charges of $4.8 million for depreciation and amortization and share-based compensation expense. Net cash used in operating activities was also impacted by $10.5 million in changes in operating assets and liabilities, including $7.5 million in prepaid expenses, $3.2 million in deferred revenue, $0.5 million in accounts receivable, $0.7 million in accounts payable and $0.4 million in other current assets and other assets, which were partially offset by changes of $1.8 million in accrued expenses.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2018 was $15.7 million, which was attributable to purchases of property, equipment and software of $14.3 million and the acquisition of intellectual property of $1.4 million.

Financing Activities

Net cash provided in financing activities for the year ended December 31, 2018 was $107.8 million, consisting of the net proceeds from the issuance of our Series B convertible preferred stock financing of $109.7 million, net of offering costs, and $0.2 million in proceeds from stock option exercises, partially offset by $2.1 million in payments for deferred offering costs associated with our initial public offering.

Loan and Security Agreement

In May 2019, we entered into the Pacific Western Loan Agreement pursuant to which we may request advances on a $50.0 million Revolving Line. The maturity date of the Revolving Line is May 15, 2022. The Revolving Line bears interest at an annual rate equal to the greater of (i) 1.25% below the prime rate then in effect, or (ii) 4.25% at all times when we maintain a daily balance of cash in our demand deposit accounts at PWB of at least $25.0 million, and the greater of (i) 0.25% above the prime rate then in effect; or (ii) 5.75% at all times when we do not maintain a daily balance of cash in demand deposit accounts at PWB of at least $25.0 million; provided that, we are permitted to maintain a bank account with a non-affiliated bank in the United Kingdom so long as the account balance does not exceed 1.5 million GBP or its U.S. dollar equivalent at any time, pursuant to the PWB Amendment. We are required to pay a fee in an amount equal to 0.50% per annum of the unused portion of the Revolving Line each quarter, or the Unused Fee. The Unused Fee shall be waived for any quarter in which we maintain a daily balance of cash in our demand deposit account at PWB of at least $25.0 million at all times during such quarter. If the Revolving Line is terminated prior to the maturity date, we are required to pay an early termination fee equal to 1.0% of the Revolving Line.

Under the terms of the Pacific Western Loan Agreement, we granted PWB a security interest in substantially all of our assets, excluding any of the intellectual property now or hereafter owned, (but including any rights to payment from the sale or licensing of any such intellectual property). We must maintain an aggregate balance of unrestricted cash and cash equivalents on hand at PWB (or PWB's affiliates) at least equal to any amounts borrowed under the Revolving Line and any other outstanding obligations the we have to PWB. The agreement was amended in December 2019 to allow a bank account with a non-affiliated bank in the United Kingdom provided that the account balance does not exceed 1.5 million GBP or its U.S. dollar equivalent at any time.

The Agreement includes customary representations, warranties and covenants (affirmative and negative), and includes standard events of default, including in the event of a material adverse change. Upon the occurrence of an event of default, PWB may declare all outstanding obligations immediately due and payable and take such other actions as are set forth in the loan and security agreement and increase the interest rate otherwise applicable to the amount outstanding under the Revolving Line by an additional 3.00%.

As of December 31, 2019, we had no borrowings under our Revolving Line, and we were in compliance with the financial covenants, under the Pacific Western Loan Agreement.

Funding Requirements

Our operating expenses increased substantially in 2019 and are expected to increase substantially in the future in connection with the initiation of additional human clinical trials and capital expenditures for MCAT.

We believe our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2021. We have based these estimates on assumptions that may prove to be imprecise, and we could utilize our available capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical and agricultural products, it is difficult to estimate with certainty the amount of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the progress, costs and results of our clinical development for our CD19, CD20, and BCMA programs as we initiate and progress clinical trials, including CRO costs;

- the progress, costs and results of our additional research and preclinical development programs;

- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities;

- the costs and timing of internal process development and manufacturing scale-up activities and contract with CMOs associated with our CD19, CD20, and BCMA programs and other programs we advance through preclinical and clinical development;

- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements;

- the scope, progress, results and costs of any product candidates that we may derive from ARCUS or any other product candidates we may develop alone or with collaborators;

- the extent to which we in-license or acquire rights to other products, product candidates or technologies;

- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims; and

- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any product candidates for which we or our collaborators obtain marketing approval.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of public or private equity or debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements and marketing and/or distribution arrangements.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, shareholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our shareholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, product development and research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations

The following is a summary of our contractual obligations and commitments as of December 31, 2019:

		Payments Due by Period			
(in thousands)	Total[2][3]	Less Than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Operating Lease Obligations[1]	$ 17,966	$ 2,706	$ 6,295	$ 5,899	$ 3,066

(1) Represents future minimum lease payments under our operating leases for office and/or lab space at the following locations: 302 East Pettigrew Street, Durham, North Carolina expiring in July 2024, 3054 Cornwallis Road, Durham, North Carolina expiring in April 2026 and 20 TW Alexander Drive, Research Triangle Park, North Carolina expiring in August 2027 (see Note 7 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information on these lease agreements).

(2) We have entered into a license agreement with an undisclosed licensee for intellectual property used in our research programs. The agreement requires us to pay annual license fees and milestones payments for achievement of specified clinical and commercial events. We have excluded these potential milestone payments in the contractual obligations table because the timing and likelihood of these contingent payments are not currently known and would be difficult to predict or estimate.

(3) This table does not reflect principal and interest payments payable pursuant to our Pacific Western Loan Agreement. which we entered into in May 2019, pursuant to which we may request advances on a revolving line of credit of up to an aggregate principal of $50.0 million, or the Revolving Line. As of December 31, 2019, we had no borrowings under our Revolving Line. The maturity date of the Revolving Line is May 15, 2022. The Revolving Line bears interest at an annual rate equal to the greater of (i) 1.25% below the prime rate then in effect, or (ii) 4.25% at all times when we maintain a daily balance of cash in our demand deposit accounts at PWB of at least $25.0 million, and the greater of (i) 0.25% above the prime rate then in effect; or (ii) 5.75% at all times when we do not maintain a daily balance of cash in demand deposit accounts at PWB of at least $25.0 million. The Pacific Western Loan Agreement requires that we pay a quarterly fee in an amount equal to 0.50% per annum of the unused portion of the Revolving Line. The unused fee shall be waived for any quarter we maintain a daily balance in our demand deposit accounts of at least $25.0 million. If the Revolving Line is terminated prior to the maturity date, we are required to pay an early termination fee equal to 1.0% of the Revolving Line.

In addition, we have entered into the Duke License, under which we are obligated to make aggregate future milestone payments of up to $0.2 million upon the achievement of specified corporate milestones as well as low-single digit percent royalty payments based on future net sales of applicable products and generally mid-teen percent royalties based on sublicensing revenue. See "Business—License and Collaboration Agreements" for more information regarding our payment obligations under the Duke License. We have not included future payments under the Duke License in the table above since the payment obligations under the Duke License are contingent upon future events, such as the achievement of specified milestones or generating product sales, and we are unable to estimate the timing or likelihood of achieving these milestones or generating future product sales.

We also enter into contracts in the normal course of business with CROs, CMOs, universities and other third parties for preclinical research studies, clinical trials and testing and manufacturing services. These contracts do not contain minimum purchase commitments and are cancelable by us upon prior written notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancellation. These payments are not included in the table above as the amount and timing of such payments are not known.

Critical Accounting Policies and Use of Estimates

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

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

Revenue Recognition

Our revenues are generated primarily through collaborative research, license, development and commercialization agreements. The terms of these agreements generally contain multiple elements, or deliverables, which may include (1) licenses, or options to obtain licenses, to use our technology, (2) research and development activities to be performed on behalf of the collaborative partner, and (3) in certain cases, services in connection with the manufacturing of preclinical and clinical material. Payments we receive under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; clinical and development, regulatory, and sales milestone payments; and royalties on future product sales. We classify payments received under these agreements as revenues within our consolidated statements of operations.

We adopted Accounting Standards Update, or ASU, No. 2014-09, *Revenue from Contracts with Customers*, or ASC 606, on January 1, 2019 using the modified retrospective transition method. Under this method, results for reporting periods beginning on January 1, 2019 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC Topic 605, *Revenue Recognition* ("ASC 605"). ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation.

At contract inception, once the contract is determined to be within the scope of ASC 606, we evaluate the performance obligations promised in the contract that are based on goods and services that will be transferred to the customer and determine whether those obligations are both (i) capable of being distinct and (ii) distinct in the context of the contract. Goods or services that meet these criteria are considered distinct performance obligations. If both these criteria are not met, the goods and services are combined into a single performance obligation. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess if these options provide a material right to the customer and, if so, these options are considered performance obligations. The exercise of a material right is accounted for as a contract modification for accounting purposes.

We recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is based on the use of an output or input method.

Amounts received prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue within current liabilities in our consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue – noncurrent. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets in the Other line item in our consolidated balance sheets.

Milestone Payments – If an arrangement includes development and regulatory milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price 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. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

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

Significant Financing Component – In determining the transaction price, we adjust consideration for the effects of the time value of money if the timing of payments provides us with a significant benefit of financing. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. We assessed each of our revenue arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in any of our arrangements.

Collaborative Arrangements – We have entered into collaboration agreements, which are within the scope of ASC 606, to discover, develop, manufacture and commercialize product candidates. The terms of these agreements typically contain multiple promises or obligations, which may include: (1) licenses, or options to obtain licenses, to use our technology, (2) research and development activities to be performed on behalf of the collaboration partner, and (3) in certain cases, services in connection with the manufacturing of preclinical and clinical material. Payments we receive under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; clinical and development, regulatory, and sales milestone payments; and royalties on future product sales.

We analyze our collaboration arrangements to assess whether they are within the scope of ASU No. 2018-18 *Collaborative Arrangements*, or ASC 808, to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, we first determine which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and, therefore, are within the scope of ASC 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to ASC 606. For those elements of the arrangement that are accounted for pursuant to ASC 606, we apply the five-step model described above.

In February 2016, we entered into the Servier Agreement for the licensing of our ARCUS proprietary genome editing platform and the research, development, and manufacturing of product for clinical trials and commercialization of products. In September 2018, we entered into a collaboration and license agreement with Gilead, which we refer to as the Gilead Agreement, to develop genome editing tools using our ARCUS proprietary genome editing platform. Both agreements use our genome editing technology for the treatment of certain diseases. Consideration we received, or may receive, under these collaboration and license agreements include upfront nonrefundable payments, research funding payments and payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

Under the guidance of ASC 606, certain judgments affect revenue recognition. Our primary performance obligations under our agreements consist of research and development services. Measuring the amount of time it takes for us to complete these services includes estimating our total effort to satisfy our performance obligations at the outset of the agreement and then comparing that amount to the actual effort expended for a given accounting period. In certain instances, significant judgment is required to estimate the timing of satisfying these obligations and timing may change due to efforts beyond our control, such as changes in the customer's direction of a particular research program or changes to the contractual terms of an agreement. Accordingly, our estimates may change in the future. Such changes to estimates will result in a change in prospective revenue recognition amounts.

Accrued Research and Development Expenses

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

- CROs and other third parties in connection with performing research and development activities, conducting preclinical studies and clinical trials on our behalf;
- Vendors in connection with preclinical development activities; and
- CMOs and other vendors in connection with product manufacturing and development and distribution of preclinical supplies.

We base our expenses related to preclinical studies on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs that conduct and manage preclinical studies and clinical trials and CMOs that manufacture product for our research and development activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may cause us to report amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Share-Based Compensation

We measure stock options and other share-based awards granted to our employees, directors, consultants and advisors based on the fair value on the date of the grant and recognize compensation expense for those awards, net of actual forfeitures, over the requisite service period, which is generally the vesting period of the respective award.

We estimate the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. As we have limited trading history, we estimate our expected volatility based on the historical volatility of publicly traded peer companies and expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded share price. The expected term of our options has been determined utilizing a weighted value considering actual history and estimated expected term based on the midpoint of final vest date and expiration date. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

Recent Accounting Pronouncements

A description of recent accounting pronouncements that may potentially impact our financial position, results of operations or cash flows is disclosed in Note 1 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

Emerging Growth Company Status

We are an "emerging growth company," as defined in the JOBS Act, and we may take advantage of reduced reporting requirements that are otherwise applicable to public companies. Section 107 of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies are required to comply with those standards. We have elected to take advantage of the extended transition period for complying with new or revised accounting standards. The JOBS Act also exempts us from having to provide an auditor attestation of internal control over financial reporting under Sarbanes-Oxley Act Section 404(b).

We will remain an "emerging growth company" until the earliest of (1) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more, (2) the last day of the fiscal year following the fifth anniversary of the completion of our IPO, (3) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years or (4) the date on which we are deemed to be a large accelerated filer under the rules of the SEC, which means the market value of our common stock held by non-affiliates exceeds $700 million as of the prior June 30th, we have been a public company for at least 12 months and have filed one Annual Report on Form 10-K.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. Our interest-earning assets consist of cash and cash equivalents, which are denominated in U.S. dollars. We had cash and cash equivalents of $180.9 million, or 77% of our total assets, at December 31, 2019 and $103.2 million, or 74% of our total assets, at December 31, 2018. Interest income earned on these assets was $4.3 million and $1.9 million for the years ended December 31, 2019 and December 31, 2018, respectively. Our interest income is sensitive to changes in the general level of interest rates, primarily U.S. interest rates. At December 31, 2019, our cash equivalents consisted of money market funds and repurchase agreements that were collateralized by deposits in the form of government securities and obligations. Such interest-earning instruments carry a degree of interest rate risk; however, we do not anticipate fluctuations in interest rates to have a significant impact on our financial statements. We had no debt outstanding as of December 31, 2019 or 2018.

We are also exposed to foreign exchange rate risk with respect to our global subsidiaries from foreign currency transactions. We do not anticipate foreign exchange rate risk to have a material impact on our financial statements.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this report and are incorporated herein by reference. An index of those financial statements is found in Item 15 of Part IV 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.

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. 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.

Evaluation of disclosure controls and procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2019.

Management's annual report on internal control over financial reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding our internal control over financial reporting or an attestation report of our independent registered accounting firm due to a transition period established by rules of the SEC for newly public companies. Additionally, our independent registered accounting firm will not be required to opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 of Sarbanes-Oxley Act of 2002 until we are no longer an "emerging growth company" as defined in the JOBS Act.

Changes in internal control over financial reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Executive Officers and Directors

The following table sets forth the name, age and position of each of our executive officers and directors as of March 2, 2020.

Name	Age	Position
Executive Officers		
Matthew Kane	43	President, Chief Executive Officer and Director
Derek Jantz, Ph.D.	44	Chief Scientific Officer and Director
Abid Ansari	42	Chief Financial Officer
Christopher Heery, M.D.	40	Chief Medical Officer
Dario Scimeca	45	General Counsel and Secretary
Fayaz Khazi, Ph.D.	47	Chief Executive Officer, Elo Life Systems
David Thomson, Ph.D.	59	Chief Operating Officer
Non-Employee Directors		
Kevin Buehler (1)(3)	62	Director
Raymond Schinazi Ph.D. (2)(3)	69	Director
Shalini Sharp (1)(2)	45	Director
Tony Yao, M.D., Ph.D. (1)(2)(3)	48	Director

(1) Member of the audit committee.

(2) Member of the compensation committee.

(3) Member of the nominating and corporate governance committee.

Executive Officers

Matthew Kane, a co-founder of Precision, has served as our President and Chief Executive Officer and a director since our inception in 2006. Mr. Kane has nearly 20 years of experience in the life sciences industry, most of which has been spent specifically working in genome editing. Prior to co-founding Precision, Mr. Kane was with Suros Surgical Systems. Mr. Kane received a B.S. in mechanical engineering and an M.S. in biomedical engineering from the Rose-Hulman Institute of Technology and an M.B.A. from Duke University.

We believe that Mr. Kane is qualified to serve on our board of directors because of the perspective and experience he provides as one of our founders and as our President and Chief Executive Officer, as well as his many years of experience within the life sciences and agricultural biotechnology industries.

Derek Jantz, *Ph.D.*, a co-founder of Precision, has been our Chief Scientific Officer since August 2013 and has served on our board of directors since January 2006. He previously served as our Vice President of Scientific Development from our inception in 2006 to August 2013. Dr. Jantz is the co-inventor of several of our foundational patents and other intellectual property. As a protein engineer, he was an early developer of zinc finger technology and has spent most of his research career designing proteins for genome editing applications. Dr. Jantz received a B.A. in biology from the University of Colorado at Boulder and a Ph.D. in biophysics from the Johns Hopkins University School of Medicine.

We believe that Dr. Jantz's extensive experience in genome editing and as an inventor of ARCUS, in addition to his perspective as one of our founders and senior executives, qualifies him to serve on our board of directors.

Abid Ansari has served as our Chief Financial Officer since February 2019. Mr. Ansari previously served as our Vice President, Finance & Operations from July 2016 to February 2019. Prior to joining us, Mr. Ansari served as Senior Director, Deal Finance and M&A from November 2013 to July 2016 and Senior Director, Head of Portfolio Analysis Group from September 2011 to November 2013 for GlaxoSmithKline plc, a multinational pharmaceutical company. Before that, he served for five years in commercial and capital finance roles at MedImmune, LLC and three years as a plant controller at Uniqema (previously a division of Imperial Chemical Industries Plc). Mr. Ansari received a B.S. in chemical engineering and an M.B.A. from Purdue University. Mr. Ansari is also a Certified Public Accountant.

Christopher Heery, M.D. has served as our Chief Medical Officer since May 2019. Prior to joining us, Dr. Heery served as Chief Medical Officer at Bavarian Nordic A/S, a biotechnology company, from October 2016 to April 2019, where he oversaw clinical development programs for its immune-oncology and infectious disease portfolios. Prior to that, he was a Staff Clinician and then an Associate Research Physician and Head of the Clinical Trials Group of the Laboratory of Tumor Immunology and Biology at the National Cancer Institute, or NCI, a U.S. government health agency, from April 2012 to November 2013 and November 2013 to September 2016, respectively, where he was part of a larger effort to create new immunotherapies for the treatment of cancer. He joined the NCI Medical Oncology Branch as a Medical Oncology Fellow in 2009 and also served as an Adjunct Appointment in the Genitourinary Malignancies Branch. Dr. Heery is board certified in Medical Oncology and Internal Medicine. He received a B.A. from Duke University and a M.D. from East Carolina University Brody School of Medicine, and completed his internal medicine residency at the University of Illinois at Chicago.

Dario Scimeca has served as our General Counsel since June 2019. Prior to joining us, Mr. Scimeca served in various roles for Genentech, a biotechnology company, U.S. affiliate of Roche, from January 2013 to June 2019, including most recently as Assistant General Counsel, where he counseled on legal issues associated with the development and commercialization of multiple drug oncology and rare disease products. Prior to that, he was corporate counsel at Elan Pharmaceuticals where he, among other things, oversaw FDA and EMA regulatory compliance matters. He has previously worked in both corporate transactional law and patent litigation at three national law firms. Mr. Scimeca received a B.S. from Santa Clara University, his J.D. from the University of California, Berkeley, School of Law, and clerked for Judge James L. Dennis on the United States Fifth Circuit Court of Appeals in New Orleans, Louisiana.

Fayaz Khazi, *Ph.D.*, has served as the CEO of our food-focused subsidiary, Elo Life Systems, since May 2018 and, prior to that, served as President of Elo Life Systems beginning in May 2017. From May 2014 to April 2017, Dr. Khazi served as the CEO of KeyGene USA, an agricultural biotechnology company. Dr. Khazi also held several executive leadership positions at Intrexon Corporation directing translation programs in the food, human health and agricultural biotechnology sectors, including serving as Vice President, Business Analytics and Strategy from January 2012 to January 2014, and also serving as Intrexon's founding Director of Translational Medicine. Dr. Khazi received a B.Sc. from the University of Agricultural Sciences, Bangalore, and a Ph.D. in biological sciences from Auburn University. He trained as a Howard Hughes Medical Institute post-doctoral fellow and a senior researcher at the Children's Hospital of Philadelphia, where he studied the genotoxicity of gene therapy vectors and developed *in vivo* genome-editing technologies to treat genetic diseases.

David Thomson, Ph.D., has served as our Chief Operating Officer since August 2019 and, prior to that, served as our Chief Development Officer beginning in June 2017. Prior to joining us, he served as Senior Vice President Research and Nonclinical Development for Shire plc, a specialty biopharmaceutical company, beginning in May 2016 until May 2017 where he was responsible for the strategy and operational direction of the Global Research and Nonclinical Development Organization, including transitioning programs from research into clinical development and support of programs through commercialization. Prior to that, he served as Senior Vice President and Global Head, Research and Development Operations for Shire from February 2015 to May 2016. From May 2014 to January 2015, Dr. Thomson served as the Director of the Biomanufacturing Research Institute and Technology Enterprise and a Professor in the Department of Pharmaceutical Sciences of North Carolina Central University. From September 2012 to April 2014, Dr. Thomson served as Vice President, Shire Human Genetic Therapies and later Senior Vice President, Global Head of Research and Nonclinical Development for Shire plc. He received a B.Sc. in chemistry from the University of Strathclyde and a Ph.D. in organic chemistry from the University of Toronto, and he completed post-doctoral work at Yale University.

Non-Employee Directors

Kevin Buehler has served on our board of directors since November 2019. Mr. Buehler has over 30 years of experience in the healthcare industry, having most recently served from April 2011 to May 2014 as the Division Head of Alcon Laboratories, Inc., a division of Novartis AG, a multinational pharmaceutical company. Prior to that, from April 2009 to April 2011, he served as the Chief Executive Officer and President of Alcon Inc., after having served from 2007 to 2009 as Alcon Inc.'s Senior Vice President, Global Markets and Chief Marketing Officer and, from 2006 to 2007, as its Senior Vice President of the U.S. market and the Chief Marketing Officer. Mr. Buehler began his career with Alcon, Inc. in August 1984. Mr. Buehler holds a B.A. degree from Carroll University in Waukesha, WI, with concentrations in Business Administration and Political Science, and is a graduate of the Harvard Executive Program for Management Development.

We believe that Mr. Buehler's more than 30 years of experience in the healthcare and industry, including both executive and board roles, qualify him to serve as member of our board of directors.

Raymond Schinazi, Ph.D., D.Sc., has served on our board of directors since March 2019. Dr. Schinazi has been the Frances Winship Walters Professor of Pediatrics and the Director of the Laboratory of Biochemical Pharmacology at Emory University, a private research university, since 2008 and 1992 respectively. From November 2014 to January 2019, Dr. Schinazi served on the board of directors of Cocrystal Pharma, Inc. Dr. Schinazi was also instrumental in the founding of a number of biotechnology companies, including Triangle Pharmaceuticals, Idenix Pharmaceuticals and Pharmasset, Inc. Dr. Schinazi currently serves on the board of directors of Brace Pharma Capital, ReViral Pharmaceuticals Ltd, Gliknik Inc., and serves on the board of trustees of amfAR, ICMEC and GVN. Dr. Schinazi is also a Charter Fellow of the National Academy of Inventors and a Fellow of the American Society of Microbiology. Dr. Schinazi received a B.Sc. and Ph.D. in chemistry and D.Sc. in biotechnology from the University of Bath.

We believe that Dr. Schinazi's medical background and biotechnology experience qualify him to serve as a member of our board of directors.

Shalini Sharp has served on our board of directors since December 2018. Since 2012, Ms. Sharp has served as Executive Vice President and Chief Financial Officer of Ultragenyx Pharmaceutical Inc., a biopharmaceutical company, holding the position of Chief Financial Officer since May 2012 and the position of Executive Vice President since January 2016. Between May 2012 and January 2016, she served as Senior Vice President of Ultragenyx. Prior to Ultragenyx, Ms. Sharp served in various executive capacities, and ultimately as Chief Financial Officer, of Agenus Inc., a biotechnology company, from August 2003 until May 2012. Ms. Sharp currently serves on the board of directors of Neurocrine Biosciences, Inc.. and Sutro Biopharma, Inc. and previously served on the board of directors of Agenus, Inc. and Array BioPharma Inc. Ms. Sharp received a B.A. in English literature and an M.B.A. from Harvard University.

We believe that Ms. Sharp's more than 20 years of experience in the life sciences industry including both executive and board roles as well as her expertise in biotechnology, corporate strategy and finance qualify her to serve as a member of our board of directors.

Tony Yao, M.D., Ph.D., has served on our board of directors since May 2018. Since April 2012, Dr. Yao has served as a portfolio manager at ArrowMark Partners, an asset management firm, where he leads the healthcare team and manages the healthcare portfolio. Dr. Yao currently serves on the board of directors of 4D Molecular Therapeutics, Inc. and NexImmune, Inc. Dr. Yao began his investment career in February 2002 as an analyst and later an assistant portfolio manager at Janus Capital Group. Dr. Yao received a Sc.B. in biochemistry from Brown University and a M.D. and Ph.D. in immunology from Stanford University.

We believe that Dr. Yao's medical background and experience in private equity investing, particularly with healthcare companies, qualify him to serve as a member of our board of directors.

Audit Committee

We have a separately designated standing audit committee. The current members of our audit committee are Kevin J. Buehler, Shalini Sharp and Tony Yao, M.D., Ph.D. Shalini Sharp serves as the chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the Nasdaq rules. Our board of directors has determined that each of Kevin J. Buehler, Shalini Sharp and Tony Yao, M.D., Ph.D. meet the independence requirements of Rule 10A-3 under the Exchange Act and the applicable Nasdaq rules. Our board of directors has determined that each of Kevin Buehler and Shalini Sharp is an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq rules.

Code of Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Our code of business conduct and ethics is available under the Corporate Governance section of our website at *www.precisionbiosciences.com*. In addition, we intend to post on our website all disclosures that are required by law or the Nasdaq rules concerning any amendments to, or waivers from, any provision of the code. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this Annual Report on Form 10-K.

Item 11. Executive Compensation.

This section discusses the material components of our 2019 compensation program for our principal executive officer and next two most highly compensated executive officers who are named in the Summary Compensation Table below. These "named executive officers" and their positions are:

- Matthew Kane, President and Chief Executive Officer;
- Christopher Heery, Chief Medical Officer; and
- Dario Scimeca, General Counsel.

Summary Compensation Table

The following table sets forth information concerning the compensation of our named executive officers for the years presented:

Name and principal position	Year	Salary ($)	Bonus ($)(1)	Option awards ($)(2)	All other compensation($)		Total ($)
Matthew Kane	2019	479,750	67,990	1,604,360	14,360	(3)	2,166,460
President and Chief Executive Officer	2018	350,000	157,500	1,068,616	11,016		1,587,132
Christopher Heery(5)							
Chief Medical Officer	2019	286,667	150,534	1,737,812	6,832	(4)	2,181,845
Dario Scimeca(7)							
General Counsel	2019	174,375	80,055	1,390,249	65,532	(6)	1,710,211

(1) The amounts reported for 2019 represent bonuses based upon our board's assessment of the achievement of company and individual performance objectives for 2019, which were paid in February 2020. For Dr. Heery and Mr. Scimeca, the amounts shown also include one-time signing bonuses of $50,000 for Dr. Heery and $35,000 for Mr. Scimeca that were paid in connection with their commencing employment with us during 2019.

(2) The amounts reported reflect the grant date fair value of stock options computed in accordance with Accounting Standards Codification 718, Compensation—Stock Compensation, or ASC 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of the option awards in Note 5 to our consolidated financial statements included in this Annual Report on Form 10-K.

(3) The amount reported includes 401(k) matching contributions by us of $10,672, nondiscriminatory life insurance premiums of $1,353, supplemental disability insurance premiums available to certain executives of $2,327, and tax gross-ups of $8 in connection with nondiscriminatory wellness and phone reimbursements for 2019.

(4) The amount reported includes 401(k) matching contributions by us of $5,733, nondiscriminatory life insurance premiums of $789, and supplemental disability insurance premiums available to certain executives of $310.

(5) Dr. Heery was not employed with the company in 2018, and accordingly, compensation information for 2018 is not included in the table above.

(6) The amount reported represents relocation and housing expenses of $45,666 and $18,853 of tax gross-ups in connection therewith, nondiscriminatory life insurance premiums of $789, supplemental disability insurance premiums available to certain executives of $207, and tax gross-ups of $17 in connection with nondiscriminatory wellness and phone reimbursements for 2019.

(7) Mr. Scimeca was not employed with the company in 2018, and accordingly, compensation information for 2018 is not included in the table above.

Annual Base Salaries

Our named executive officers receive a base salary to compensate them for services rendered to us. The base salary payable to each named executive officer is intended to provide a fixed component of compensation reflecting the executive's skill set, experience, role and responsibilities. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary. The following table shows the annual base salaries for 2019 of our named executive officers:

Name	2019 Base salary ($)
Matthew Kane(1)	523,000
Christopher Heery	430,000
Dario Scimeca	310,000

(1) Mr. Kane's annual base salary was increased from $350,000 to $523,000 in connection with our IPO.

Bonuses

In addition to base salaries, our named executive officers were eligible to receive a cash bonus based on company and individual performance for 2019. The performance objectives for 2019 cash bonuses related to attaining certain clinical and non-clinical milestones, as well as financial and administrative achievements. In connection with our IPO, the target bonus amount for Mr. Kane was set at 50% of his base salary. The target bonus amount for Dr. Heery and Mr. Scimeca is 35% of their respective base salaries.

The actual bonus amounts paid to our named executive officers for 2019 are set forth above in the 2019 Summary Compensation Table in the column entitled "Bonus."

In addition to their 2019 annual bonuses, Dr. Heery and Mr. Scimeca received sign-on bonuses of $50,000 and $35,000, respectively, in connection with commencing employment with us during 2019. Each sign-on bonus is subject to repayment in the event the executive voluntarily resigns or is terminated for cause within the first year of employment.

Equity Compensation

Our equity award program is the primary vehicle for offering long-term incentives to our executives. We believe that equity awards provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. To date, we have used stock option grants for this purpose because we believe they are an effective means by which to align the long-term interests of our executive officers with those of our stockholders. The use of options also can provide tax and other advantages to our executive officers relative to other forms of equity compensation. We believe that our equity awards are an important retention tool for our executive officers, as well as for our other employees.

We award stock options broadly to our employees, including to our non-executive employees. Grants to our executives and other employees are made at the discretion of our board of directors and are not made at any specific time period during a year.

In connection with our IPO, we adopted our 2019 Incentive Award Plan, referred to as the 2019 Plan, to facilitate the grant of cash and equity incentives to directors, employees (including our named executive officers) and consultants of our company and to enable our company to obtain and retain services of these individuals, which we believe are essential to our long-term success. Following the effectiveness of our 2019 Plan, we ceased making grants under our 2015 Plan. However, our 2015 Plan continues to govern the terms and conditions of the outstanding awards granted under it.

We granted the following stock options to our named executive officers during 2019 under our 2019 Plan:

Named executive officers	Stock options granted
Matthew Kane(1)	262,252
Christopher Heery(2)	200,000
Dario Scimeca(3)	160,000

(1) The option vests as to 25% of the underlying shares on April 1, 2020 and vests in equal installments at the end of each successive three-month period over the 36 months following such date.

(2) The option vests as to 25% of the underlying shares on May 1, 2020 and vests in equal installments at the end of each successive three-month period over the 36 months following such date.

(3) The option vests as to 25% of the underlying shares on June 10, 2020 and vests in equal installments at the end of each successive three-month period over the following 36 months.

Retirement Plans

We currently maintain the Precision BioSciences, Inc. 401(k) Plan, a defined contribution retirement savings plan, or the 401(k) Plan, for the benefit of our employees, including our named executive officers, who satisfy certain eligibility requirements. Our named executive officers are eligible to participate in the 401(k) Plan on the same terms as other full-time employees. The Code allows eligible employees to defer a portion of their compensation, within prescribed limits, on a pre-tax basis through contributions to the 401(k) Plan. In 2019, we matched participants' elective salary deferral contributions to the 401(k) Plan up to 100% of the first 4% of the employee's salary deferred. Matching contributions made by us vest immediately. We believe that providing a vehicle for tax-deferred retirement savings though our 401(k) Plan, and making matching contributions, adds to the overall desirability of our executive compensation package and further incentivizes our employees, including our named executive officers, in accordance with our compensation policies.

Employee Benefits and Perquisites

Our named executive officers are eligible to participate in our employee benefit plans and programs, which include medical, dental and vision benefits, health and flexible spending accounts, life, short-term, long-term and supplemental individual disability, and supplemental insurance and wellness and tuition reimbursement to the same extent as our other full-time employees generally, subject to the terms and eligibility requirements of those plans. We also provide Messrs. Kane and Scimeca and Dr. Heery, along with certain other executive officers and senior employees, with certain supplemental disability insurance benefits. We also provide relocation benefits to our named executive officers as determined in our board's discretion.

Outstanding Equity Awards at 2019 Fiscal Year-End

The following table summarizes the number of shares of common stock underlying outstanding equity incentive plan awards for each of our named executive officers as of December 31, 2019.

	Option awards			
Name	Number of securities underlying unexercised options (#) exercisable	Number of securities underlying unexercised options (#) unexercisable	Option exercise price ($)	Option expiration date
Matthew Kane	322,711	—	0.04	5/17/2021
	6,104	7,318 (1)	1.18	3/23/2027
	43,917	96,618 (2)	11.98	9/27/2028
	—	262,252 (3)	9.46	9/22/2029
Christopher Heery	—	200,000 (4)	13.39	7/3/2029
Dario Scimeca	—	160,000 (5)	13.39	7/3/2029

(1) The option vested as to 25% of the underlying shares on March 24, 2018 and vests in equal installments at the end of each successive three-month period over the following 36 months.

(2) The option vested as to 25% of the underlying shares on September 28, 2019 and vests in equal installments at the end of each successive three-month period over the following 36 months.

(3) The option vests as to 25% of the underlying shares on April 1, 2020 and vests in equal installments at the end of each successive three-month period over the following 36 months.

(4) The option vests as to 25% of the underlying shares on May 1, 2020 and vests in equal installments at the end of each successive three-month period over the following 36 months.

(5) The option vests as to 25% of the underlying shares on June 10, 2020 and vests in equal installments at the end of each successive three-month period over the following 36 months.

Employment Agreements

We have entered into employment agreements with each of our named executive officers that set forth the terms and conditions of each executive's employment with us.

Each employment agreement establishes an annual base salary and target bonus opportunity for each named executive officer, the current amounts of which are described above under the headings "Annual Base Salaries" and "Bonuses". The named executive officers are eligible to participate in our medical, dental and disability insurance, the 401(k), personal leave and other employee benefit plans and programs for which the named executive officer is eligible, subject to the terms and conditions of such plans and programs.

Each named executive officer's employment agreement and employment are terminable by either the named executive officer or us without cause on 30-days' notice. In the event that a named executive officer's employment is terminated by us without cause or by the executive for good reason, in each case as defined in the employment agreements, then in addition to payment of any accrued amounts and subject to such named executive officer's timely executing a release of claims and continuing to comply with obligations under his proprietary information agreement, he will be entitled to receive (1) base salary continuation for 12 months in the case of Mr. Kane or nine months in the case of Dr. Heery and Mr. Scimeca, and (2) reimbursement for additional costs the executive incurs for continued coverage under our group health insurance under the Consolidated Budget Reconciliation Act of 1985, or COBRA, for up to 12 months in the case of Mr. Kane or nine months in the case of Dr. Heery and Mr. Scimeca.

In lieu of the foregoing, the employment agreements provide that, in the event a named executive officer's employment is terminated by us without cause or by the named executive officer for good reason three months prior to or 12 months after the occurrence of a change in control, then, subject to his timely executing a release of claims and continuing to comply with obligations under his proprietary information agreement, then such named executive officer shall be entitled to (1) a lump sum payment equal to, in the case of Mr. Kane, 18 months of his then current base salary plus 1.5 times his target bonus, and in the case of Dr. Heery and Mr. Scimeca, 12 months of base salary plus one times his target bonus, (2) reimbursement for the additional costs the executive incurs for continued coverage under our group health insurance under COBRA for up to 18 months in the case of Mr. Kane and up to 12 months in the case of Dr. Heery and Mr. Scimeca, and (3) accelerated vesting of all unvested time-based equity grants.

Under the separate proprietary information, inventions, non-competition and non-solicitation agreement with each of Mr. Kane, Dr. Heery and Mr. Scimeca, referred to as the proprietary information agreement above, each named executive officer has agreed to refrain from competing with us or soliciting our employees, independent contractors, customers or suppliers, in each case, while employed and following the termination of his employment for any reason for a period of one year. Notwithstanding the foregoing, no such post-employment restrictions are intended to restrain Mr. Scimeca's ability to practice law or violate any rules of professional conduct to which he is subject. Each named executive officer has acknowledged our ownership rights in any intellectual property and assigned any such ownership rights to us.

Director Compensation

2019 Option Grants to Non-Employee Directors

In connection with our IPO, Dr. Schinazi was granted an option to purchase 34,544 shares, which option will vest as to 34% of the underlying shares on March 27, 2020 and in equal installments at the end of each three-month period over the following 24 months. In November 2019 in connection with his election to our board, Mr. Buehler was granted an option as an initial award under our non-employee director compensation program to purchase 60,776 shares of common stock. This option vests in 36 substantially equal monthly installments following November 8, 2019.

Non-Employee Director Compensation Policy

In connection with our IPO, we adopted and our stockholders approved a compensation program for our non-employee directors under which each non-employee director is eligible to receive the following amounts for their services on our board of directors:

- Upon the director's initial election or appointment to our board of directors, an option to purchase shares of our common stock having an aggregate fair value of $350,000 (as determined under the policy);
- If the director has served on our board of directors for at least six months as of the date of an annual meeting of stockholders and will continue to serve as a director immediately following such meeting, an option to purchase shares of our common stock on the date of the annual meeting having an aggregate fair value of $175,000 (as determined under the policy);
- An annual director fee of $40,000;
- If the director serves on a committee of our board of directors, an additional annual fee as follows:
    - Chairman of the audit committee, $15,000;
    - Audit committee member other than the chairman, $7,500;
    - Chairman of the compensation committee, $12,250;
    - Compensation committee member other than the chairman, $6,000;
    - Chairman of the nominating and corporate governance committee, $8,250; and
    - Nominating and corporate governance committee member other than the chairman, $4,500.

Director fees under the program are payable in arrears in four equal quarterly installments not later than the fifteenth day following the final day of each calendar quarter, provided that the amount of each payment will be prorated for any portion of a quarter that a director is not serving on our board.

Stock options granted to our non-employee directors under the program have an exercise price equal to the fair market value of our common stock on the date of grant and expire not later than ten years after the date of grant. The stock options granted upon a director's initial election or appointment vest in thirty-six substantially equal monthly installments following the date of grant. The stock options granted annually to directors vest in a single installment on the earlier of the day before the next annual meeting or the first anniversary of the date of grant. In addition, all unvested stock options vest in full upon the occurrence of a change in control.

2019 Director Compensation

The following table sets forth the compensation earned by our non-employee directors for their service on our board during 2019:

Name	Fees earned or paid in cash ($)	Option awards ($)(1)	Total ($)
Kevin Buehler	8,363	353,599	361,962
Raymond Schinazi, Ph.D.	43,195	283,081	326,276
Shalini Sharp	55,178	—	55,178
Tony Yao, M.D., Ph.D. (2)	29,644	—	29,644

(1) The amounts reported reflect the grant date fair value of stock options computed in accordance with Accounting Standards Codification 718, Compensation—Stock Compensation, or ASC 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of the option awards in Note 5 to our consolidated financial statements included in this Annual Report.

(2) The amount shown represents cash fees earned by Dr. Yao for his service on our board during 2019. Due to his association with ArrowMark Funds (as defined below), Dr. Yao is not permitted to receive compensation for his service on our board and elected to forego $29,000 of such fees. Dr. Yao was not granted options to purchase shares of our common stock during 2019.

The table below shows the aggregate numbers of option awards held as of December 31, 2019 by each non-employee director who was serving as of December 31, 2019.

	Option Awards	
Name	Number of securities underlying unexercised options (#) vested	Number of securities underlying unexercised options (#) unvested
Kevin Buehler	1,688	59,088
Raymond Schinazi, Ph.D.	2,928	40,985
Shalini Sharp	50,171	97,391
Tony Yao, M.D., Ph.D.	—	—

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

Equity Compensation Plan Information

The following table provides information on our equity compensation plans as of December 31, 2019.

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights (a)		Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights (b)		Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (excluding securities reflected in column (a))(4) (c)
Equity Compensation Plans Approved by Stockholders [1]	8,919,116	(2)	$ 7.02	(3)	3,204,041
Equity Compensation Plans Not Approved by Stockholders	—		—		—
Total	8,919,116		$ 7.02		3,204,041

(1) Consists of the Company's 2006 Stock Incentive Plan, as amended (the "2006 Plan"), 2015 Stock Incentive Plan, as amended (the "2015 Plan"), 2019 Incentive Award Plan (the "2019 Plan") and 2019 Employee Stock Purchase Plan (the "2019 ESPP").

(2) Includes 1,385,203 outstanding options to purchase shares of our common stock under the 2006 Plan, 5,462,954 outstanding options to purchase shares of our common stock under the 2015 Plan and 2,070,959 outstanding options to purchase shares of our common stock under the 2019 Plan. Excludes purchase rights accruing under the 2019 ESPP.

(3) As of December 31, 2019, the weighted-average exercise price of outstanding options under the 2006 Plan was $0.04, under the 2015 Plan was $7.27, and under the 2019 Plan was $11.05.

(4) Includes 2,679,041 shares available for future issuance under the 2019 Plan and 525,000 shares available for future issuance under the 2019 ESPP (of which 44,197 shares were issued with respect to the purchase period in effect as of December 31, 2019, which ended February 29, 2020). The 2019 Plan provides for an annual increase on the first day of each calendar year beginning on January 1, 2020 and ending on and including January 1, 2029 equal to the lesser of (A) 4% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (B) such smaller number of shares as is determined by the board. The number of shares available for issuance under the 2019 ESPP will be annually increased on the first day of each calendar year beginning on January 1, 2020 and ending on and including January 1, 2029, by an amount equal to the lesser of (A) 1% of the shares of common stock outstanding on the final day of the immediately preceding calendar year and (b) such smaller number of shares of common stock as determined by the board. The 2006 Plan expired in accordance with its terms in May 2016, and no further stock awards may be granted under the 2006 Plan. Additionally, following the effective date of the 2019 Plan, we ceased making grants under the 2015 Plan. To the extent outstanding stock options under the 2006 Plan or the 2015 Plan are forfeited or lapse unexercised, the shares of common stock subject to such stock options will be available for issuance under the 2019 Plan**.**

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth information with respect to the beneficial ownership of our common stock as of March 2, 2020 by:

- each person or group of affiliated persons known by us to beneficially own more than 5% of our common stock;
- each of our named executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

The number of shares beneficially owned by each individual or entity listed in the table below is determined under rules promulgated by the SEC. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power, which includes the power to dispose of or to direct the disposition of such security. In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of such person, shares of common stock subject to options or other rights held by such person that are currently exercisable or will become exercisable within 60 days of March 2, 2020 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless otherwise noted, the address of all listed individuals or entities is c/o Precision BioSciences, 302 East Pettigrew St., Suite A-100, Durham, North Carolina 27701. Each of individual and entity listed has sole voting and investment power with respect to the shares beneficially owned by such person unless otherwise noted, subject to community property laws where applicable.

Name of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
5% or Greater Shareholders		
venBio Global Strategic Fund, L.P. (1)	4,265,141	8.3%
Derek Jantz, Ph.D. (2)	4,216,178	8.2%
Capital World Investors (3)	4,062,000	7.9%
FMR LLC (4)	2,630,134	5.1%
Named Executive Officers and Directors		
Matthew Kane (5)	2,298,656	4.4%
Christopher Heery, M.D. (6)	52,485	*
Dario Scimeca (7)	2,072	*
Kevin J. Buehler (8)	8,440	*
Raymond F. Schinazi, Ph.D. (9)	108,306	*
Shalini Sharp (10)	62,345	*
Tony Yao, M.D., Ph.D. (11)	160,416	*
All executive officers and directors as a group (11 persons) (12)	7,522,381	14.3%

* Represents less than 1%.

(1) Based on information reported on a Schedule 13D filed on April 9, 2019, each of venBio Global Strategic Fund, L.P. (the "Fund"), venBio Global Strategic GP, L.P. (the "General Partner"), venBio Global Strategic GP, Ltd. (the "GP Ltd.") and Robert Adelman and Corey Goodman (collectively, the "Directors") have shared voting power and shared dispositive power over 4,265,141 shares of our common stock. The Fund directly holds 4,265,141 shares of our common stock. As the sole general partner of the Fund, the General Partner may be deemed to beneficially own the shares held by the Fund and as the sole general partner of the General Partner, the GP Ltd. may be deemed to beneficially own the shares held by the Fund. As directors of the GP Ltd., each of the Directors may be deemed to beneficially own the shares held by the Fund. The business address of each of the reporting persons listed in this footnote is 1700 Owens Street, Suite 595, San Francisco, CA 94158.

(2) Consists of (a) 3,858,346 shares of common stock and (b) 357,832 shares of common stock underlying options exercisable within 60 days of March 2, 2020.

(3) Based on information reported on a Schedule 13G filed on February 14, 2020, Capital World Investors, a division of Capital Research and Management Company (CRMC), has sole voting power and sole dispositive power over 4,062,000 shares of our common stock. The business address of Capital World Investors is 333 South Hope Street, Los Angeles, CA 90071.

(4) Based on information reported on a Schedule 13G/A filed on February 7, 2020, FMR LLC has sole voting power over 2,534,287 shares of our common stock and sole dispositive power over 2,630,134 shares of our common stock, and Abigail P. Johnson has sole dispositive power over 2,630,134 shares of our common stock. The business address of each of the reporting persons listed in this footnote is 245 Summer Street, Boston, Massachusetts 02210.

(5) Consists of (a) 1,815,922 shares of common stock held directly by Mr. Kane, (b) 8,718 shares of common stock held by Chelsea Lynam, Mr. Kane's wife, (c) 448,542 shares of common stock underlying options held by Mr. Kane exercisable within 60 days of March 2, 2020 and (d) 25,474 shares of common stock underlying options held by Ms. Lynam exercisable within 60 days of March 2, 2020.

(6) Consists of (a) 2,485 shares of common stock and (b) 50,000 shares of common stock underlying options exercisable within 60 days of March 2, 2020.

(7) Consists of 2,072 shares of common stock.

(8) Consists of (a) 8,440 shares of common stock underlying options exercisable within 60 days of March 2, 2020.

(9) Consists of (a) 93,048 shares of common stock held by RFS Partners, LP, or RFS. RFS & Associates, LLC, or RFS & Associates, is the general partner of RFS and Dr. Schinazi is a limited partner of RFS as well as the manager of RFS & Associates. Dr. Schinazi may be considered the beneficial owner of the shares held by RFS and disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The principal business address of RFS is 1860 Montreal Road, Tucker, GA 30084 and (b) 15,258 shares of common stock underlying options held by Dr. Schinazi exercisable within 60 days of March 2, 2020.

(10) Consists of 62,345 shares of common stock underlying options exercisable within 60 days of March 2, 2020.

(11) Consists of (a) 4,450 shares of common stock held directly by Dr. Yao, (b) 151,516 shares of common stock held by ArrowMark Life Science Fund, LP, or ArrowMark Fund, and (c) 4,450 shares of common stock held by THB Iron Rose, LLC Life Science Portfolio, or THB Fund. ArrowMark Colorado Holdings LLC, or ArrowMark Colorado, is an investment advisor to ArrowMark Fund and THB Fund. Dr. Yao, one of our directors, is employed as a portfolio manager for ArrowMark Colorado and has direct voting and dispositive control over the shares held by ArrowMark Fund and THB Fund. Dr. Yao may be considered the beneficial owner of the shares held by ArrowMark Fund and THB Fund and disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The principal business address of ArrowMark Fund and THB Fund is 100 Fillmore Street, Suite 325, Denver, Colorado 80206.

(12) Consists of (a) 6,184,909 shares of common stock and (b) 1,337,472 shares of common stock underlying options exercisable within 60 days of March 2, 2020.

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

Our board of directors recognizes that transactions with related persons present a heightened risk of conflicts of interests and/or improper valuation (or the perception thereof). Our board of directors has adopted a written policy on transactions with related persons, which requires that our audit committee approve or ratify related person transactions required to be disclosed pursuant to Item 404(a) or, if applicable, Item 404(d) of Regulation S-K. Item 404 of Regulation S-K requires disclosure, subject to certain exceptions, of transactions in which we were or are to be a participant and the amount involved exceeds $120,000 (or such other amount is applicable while we remain a smaller reporting company) and in which any "related person" as defined under Item 404(a) of Regulation S-K had or will have a direct or indirect material interest). It is our policy that directors interested in a related person transaction will recuse themselves from any vote on a related person transaction in which they have an interest. Each of the transactions described below entered into following the adoption of our related person transaction policy was approved in accordance with such policy.

Duke License

As more fully described in Part I, Item 1. "Business—License and Collaboration Agreements—Duke University," we are party to the Duke License, pursuant to which Duke granted us an exclusive license (subject to certain exceptions) under certain patents owned by Duke related to certain meganucleases and methods of making such meganucleases. The patents in-licensed by us from Duke pursuant to the Duke License were invented by Dr. Jantz, one of our executive officers, a director and a beneficial owner of more than 5% of our common stock, Jeff Smith, Ph.D., one of our employees and formerly a beneficial owner of more than 5% of our common stock, and another inventor who is not affiliated with us.

Pursuant to Duke's inventors' policy, inventors of intellectual property invented at Duke, including the inventors of patents licensed to us under the Duke License, are entitled to a portion of the income derived from such inventions. Accordingly, Drs. Jantz and Smith are entitled to receive a portion of the amounts we pay to Duke under the Duke License, together with amounts received by Duke from sales of common stock that we issued to Duke at the inception of the Duke License, are payable by Duke directly to Drs. Jantz and Smith. In connection with the Duke License, Drs. Jantz and Smith each received $284,869 from Duke during the year ended December 31, 2018, and each received $440,625 from Duke during the year ended December 31, 2019.

Participation in our Initial Public Offering

In connection with our IPO, certain of our stockholders and members of our board of directors purchased shares of our common stock from the underwriters at the initial public offering price of $16.00 per share, and on the same terms as other investors in our IPO. The following table summarizes purchases of shares of our common stock in our IPO by beneficial owners of more than 5% of our capital stock and entities affiliated with members of our board of directors.

Participants	Shares Purchased	Total Purchase Price
5% or greater stockholders and directors		
F-Prime Capital Partners Healthcare Fund IV LP	50,000	$ 800,000
RA Capital Healthcare Fund, L.P.	250,000	$ 4,000,000
venBio Global Strategic Fund, L.P.(1)	50,000	$ 800,000

(1) Robert Adelman, M.D., a former member of our board of directors, is a partner at venBio Global Strategic Fund, L.P.

Series B Preferred Stock Financing

From May 2018 to July 2018, we issued and sold to investors in a private placement 21,956,095 shares of our Series B preferred stock at a price per share of $5.01, for aggregate gross proceeds of $110.0 million.

The following table summarizes the Series B preferred stock purchased by directors, executive officers, then beneficial owners of more than 5% of our capital stock or any member of the immediate family of any of the foregoing persons.

Participants	Series B Preferred Stock	Total Purchase Price
5% or greater stockholders and directors		
Amgen Investments Ltd.(1)	499,002	$ 2,500,000
F-Prime Capital Partners Healthcare Fund IV LP(2)	873,253	$ 4,374,997
RA Capital Healthcare Fund, L.P.	399,202	$ 2,000,002
venBio Global Strategic Fund, L.P.(3)	998,004	$ 5,500,000
Tony Yao(4)	9,500	$ 47,595
RFS Partners, LP(5)	119,761	$ 600,003

(1) Series B preferred stock was purchased by Amgen Ventures LLC, an affiliate of Amgen Investment Ltd.

(2) Ben Auspitz, a former member of our board of directors, is a partner at F-Prime Capital Partners, a fund affiliated with FMR LLC. Mr. Auspitz does not hold voting or dispositive power over the shares held by F-Prime Capital Partners Healthcare Fund IV LP. See Part III, Item 12. “Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters” for more information.

(3) Robert Adelman, M.D., a former member of our board of directors, is a partner at venBio Global Strategic Fund, L.P. See Part III, Item 12. “Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters” for more information.

(4) Tony Yao, M.D., Ph.D. is a current member of our board of directors. Dr. Yao is associated with the ArrowMark Funds (as defined below). See Part III, Item 12. “Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters” for more information.

(5) Raymond Schinazi, Ph.D. is a current member of our board of directors. Dr. Schinazi is associated with RFS Partners, LP. See Part III, Item 12. “Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters” for more information.

Convertible Note Financing

In March 2019, we sold and issued $39.6 million aggregate principal amount of convertible notes payable, or the 2019 Notes, in a private placement transaction. ArrowMark Fundamental Opportunity Fund, L.P. purchased $0.6 million of 2019 Notes, and ArrowMark Life Science Fund, L.P. purchased $0.5 million of 2019 Notes. Tony Yao, M.D., Ph.D. is a current member of our board of directors and is associated with the ArrowMark Funds (as defined below). RFS Partners, LP purchased $0.5 million of 2019 Notes. Raymond Schinazi, Ph.D. is a current member of our board of directors and is associated with RFS Partners, LP.

The 2019 Notes converted into 2,921,461 shares of common stock immediately prior to the closing of our IPO.

Investors' Rights Agreement

We are party to an amended and restated investors' rights agreement, as amended, which we refer to as our investors' rights agreement, with each holder of our convertible preferred stock and 2019 Notes and certain holders of our common stock (Derek Jantz, Matthew Kane and Jeff Smith), which includes each holder of more than 5% of our capital stock and certain of our directors (Matthew Kane, Derek Jantz, Raymond Schinazi and Tony Yao, M.D., Ph.D.) (or, in some cases, entities affiliated therewith). Our investors' rights agreement imposes certain affirmative obligations on us and also grants certain rights to the holders, including certain registration rights with respect to the registrable securities held by them that survived our IPO.

Director and Officer Indemnification and Insurance

We have agreed to indemnify each of our directors and executive officers against certain liabilities, costs and expenses and have purchased directors' and officers' liability insurance.

Employment Agreements

We have entered into employment agreements with certain of our executive officers, including our named executive officers. For more information regarding the agreements with our named executive officers, see Part III, Item 11, "Executive Compensation—Employment Agreements."

Stock Option Grants to Executive Officers and Directors

We have granted stock options to our executive officers as more fully described in Part III, Item 11, "Executive Compensation."

Other Transactions

Chelsea Lynam, Mr. Kane's wife, serves as our Manager, Facilities Planning & Design. Ms. Lynam earned total compensation of $273,375 in 2018 in respect of base salary, bonus and the grant date fair value of options to purchase 28,106 shares of our common stock. Ms. Lynam earned total compensation of $111,518 in 2019 in respect of base salary and bonus. Ms. Lynam also participates in other employee benefit plans and arrangements that are made generally available to other employees.

Director Independence

Our board of directors has determined that, of our six directors serving as of March 2, 2020, Kevin Buehler, Raymond Schinazi Ph.D., Shalini Sharp and Tony Yao, M.D., Ph.D. do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the applicable listing rules of The Nasdaq Stock Market LLC, or the Nasdaq rules. Furthermore, the board of directors determined that, during his service as a director during 2019, Robert Adelman, M.D., qualified as an independent director under applicable Nasdaq rules. There are no family relationships among any of our directors or executive officers.

Item 14. Principal Accountant Fees and Services.

The following table summarizes the fees of Deloitte & Touche LLP, our independent registered public accounting firm, billed to us in each of the last two fiscal years (in thousands):

Fee Category	2019	2018
Audit fees	$ 589	$ 1,428
Tax fees	25	62
All other fees	2	2
Total	$ 616	$ 1,492

Audit Fees

Audit fees consisted of the following:

- Fees for the audit of our consolidated financial statements, the review of the unaudited interim financial statements included in our quarterly reports on Form 10-Q and other professional services provided in connection with statutory and regulatory filings or engagements.

- Fees for assurance and related services that are reasonably related to the performance of the audit or review of the registrant's financial statements, including for assurance reporting on our historical financial information included in our SEC registration statement in connection with our initial public offering.

Tax Fees

Tax fees consisted of fees for tax compliance, tax advice, and tax planning services.

All Other Fees

All other fees consisted of subscription fees for accounting research software.

Audit Committee Pre-Approval Policy and Procedures

The formal written charter for our audit committee requires that the audit committee pre-approve all audit services to be provided to us, whether provided by our principal auditor or other firms, and all other services (review, attest and non-audit) to be provided to us by our independent registered public accounting firm, other than *de minimis* non-audit services approved in accordance with applicable SEC rules.

The audit committee has adopted a policy (the "Pre-Approval Policy") that sets forth the procedures and conditions pursuant to which audit and non-audit services proposed to be performed by our independent registered public accounting firm may be pre-approved. The Pre-Approval Policy generally provides that the audit committee will not engage an independent registered public accounting firm to render any audit, audit-related, tax or permissible non-audit service unless the service is either (i) explicitly approved by the audit committee ("specific pre-approval") or (ii) entered into pursuant to the pre-approval policies and procedures described in the Pre-Approval Policy ("general pre-approval"). Unless a type of service to be provided by our independent registered public accounting firm has received general pre-approval under the Pre-Approval Policy, it requires specific pre-approval by the audit committee or by a designated member of the audit committee to whom the committee has delegated the authority to grant pre-approvals. Any member of the audit committee to whom the committee delegates authority to make pre-approval decisions must report any such pre-approval decisions to the audit committee at its next scheduled meeting. If circumstances arise where it becomes necessary to engage the independent registered public accounting firm for additional services not contemplated in the original pre-approval categories or above the pre-approved amounts, the audit committee requires pre-approval for such additional services or such additional amounts. Any proposed services exceeding pre-approved cost levels or budgeted amounts will also require specific pre-approval. For both types of pre-approval, the audit committee will consider whether such services are consistent with the SEC's rules on auditor independence.

On an annual basis, the audit committee reviews and generally pre-approves the services (and related fee levels or budgeted amounts) that may be provided by our independent registered accounting firm without first obtaining specific pre-approval from the Audit Committee. The audit committee may revise the list of general pre-approved services from time to time, based on subsequent determinations.

The services provided to us by Deloitte & Touche LLP in 2019 and 2018 were provided in accordance with our pre-approval policies and procedures, as then applicable.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a)(1) Financial Statements

The following documents are included on pages F-1 through F-24 attached hereto and are filed as part of this Annual Report on Form 10-K.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

(a)(2) Financial Statement Schedules

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(a)(3) Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Index

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed Herewith
3.1	Amended and Restated Certificate of Incorporation of Precision BioSciences, Inc.	8-K	001-38841	3.1	4/1/2019	
3.2	Amended and Restated Bylaws of Precision BioSciences, Inc.	8-K	001-38841	3.2	4/1/2019	
4.1	Specimen Common Stock Certificate	S-1/A	333-230034	4.1	3/18/2019	
4.2	Amended and Restated Investors' Rights Agreement among Precision BioSciences, Inc. and certain of its stockholders and the holders of the 2019 Notes, dated May 25, 2018, as amended	S-1/A	333-230034	4.2	3/18/2019	
4.3	Amendment No. 2, dated February 3, 2020, to the Amended and Restated Investors' Rights Agreement among Precision BioSciences, Inc. and certain of its stockholders and the holders of the 2019 Notes, dated May 25, 2018, as amended	8-K	001-38841	10.1	2/6/2020	
4.4	Description of the Registrant's Securities					*
10.1	Loan and Security Agreement, dated May 15, 2019, among Precision BioSciences, Inc., Elo Life Systems, Inc. and Pacific Western Bank	8-K	001-38841	10.1	5/20/2019	
10.2	First Amendment, dated September 18, 2019, to Loan and Security Agreement, dated May 15, 2019, among Precision BioSciences, Inc., Elo Life Systems, Inc. and Pacific Western Bank	10-Q	001-38841	10.1	11/12/2019	
10.3	Second Amendment, dated December 3, 2019, to Loan and Security Agreement, dated May 15, 2019, among Precision BioSciences, Inc., Elo Life Systems, Inc. and Pacific Western Bank					*
10.4†	Development and Commercial License Agreement by and between Les Laboratoires Servier and Precision BioSciences, Inc., dated February 24, 2016, as amended	S-1	333-230034	10.1	3/1/2019	
10.5††	Amendment No. 5, dated September 18, 2019, to Development and Commercial License Agreement by and between Les Laboratoires Servier and Precision BioSciences, Inc., dated February 24, 2016, as amended	10-Q	001-38841	10.2	11/12/2019	
10.6†	License Agreement by and between Duke University and Precision BioSciences, Inc., dated April 17, 2006, as amended	S-1	333-230034	10.2	3/1/2019	
10.7†	Patent Cross-License Agreement by and between Cellectis SA and Precision BioSciences, Inc., dated January 23, 2014	S-1	333-230034	10.3	3/1/2019	
10.8†	Collaboration and License Agreement by and between Gilead Sciences, Inc. and Precision BioSciences, Inc., dated September 10, 2018	S-1/A	333-230034	10.4	3/13/2019	
10.9	Lease Agreement between Precision BioSciences, Inc. and Venable Tenant, LLC, dated April 5, 2010, as amended					*
10.10	Lease Agreement between Elo Life Systems, Inc. and ARE-NC Region No. 17, LLC, dated March 29, 2018, as amended	S-1	333-230034	10.6	3/1/2019	
10.11	Lease Agreement between Precision BioSciences, Inc. and Durham TW Alexander, LLC, dated October 2, 2018, as amended					*
10.12#	2006 Stock Incentive Plan, as amended, and form of award agreements thereunder	S-1	333-230034	10.8	3/1/2019	

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed Herewith
10.13#	2015 Stock Incentive Plan, as amended, and form of award agreements thereunder	S-1	333-230034	10.9	3/1/2019	
10.14#	2019 Incentive Award Plan, and forms of award agreements thereunder	S-1/A	333-230034	10.10	3/18/2019	
10.15#	2019 Employee Stock Purchase Plan	S-1/A	333-230034	10.11	3/18/2019	
10.16#	Employment Agreement between Precision BioSciences, Inc. and Matthew Kane, dated February 27, 2019	S-1/A	333-230034	10.12	3/18/2019	
10.17#	Employment Agreement between Precision BioSciences, Inc. and Derek Jantz, dated February 27, 2019	S-1/A	333-230034	10.13	3/18/2019	
10.18#	Employment Agreement between Precision BioSciences, Inc. and Abid Ansari, dated February 27, 2019	S-1/A	333-230034	10.14	3/18/2019	
10.19#	Employment Agreement between Precision BioSciences, Inc. and David Thomson, dated February 27, 2019, as amended					*
10.20#	Employment Agreement between Precision BioSciences, Inc. and Fayaz Khazi, dated February 27, 2019	S-1/A	333-230034	10.16	3/18/2019	
10.21#	Employment Agreement between Precision BioSciences, Inc. and Christopher Ryan Heery, dated April 1, 2019					*
10.22#	Employment Agreement between Precision BioSciences, Inc. and Dario, Scimeca dated April 11, 2019					*
10.23#	Form of Indemnification Agreement between Precision BioSciences, Inc. and its directors and officers	S-1A	333-230034	10.17	3/18/2019	
10.24#	Non-Employee Director Compensation Plan	S-1A	333-230034	10.18	3/18/2019	
21.1	Subsidiaries of Precision BioSciences, Inc.					*
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 Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					*
31.2	Certification of Principal Financial Officer Pursuant to 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.					*
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	XBRL Instance Document					*
101.SCH	XBRL Taxonomy Extension Schema Document					*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					*
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					*

* Filed herewith
** Furnished herewith
† Confidential treatment of certain provisions has been granted by the SEC pursuant to Rule 406 under the Securities Act of 1933, as amended.
†† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.
# Denotes a management contract or compensation plan or arrangement

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Company Name

Date: March 10, 2020

By: /s/Matthew Kane
Matthew Kane
President, Chief Executive Officer and Director

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/Matthew Kane **Matthew Kane**	President, Chief Executive Officer and Director (*principal executive officer*)	March 10, 2020
/s/Abid Ansari **Abid Ansari**	Chief Financial Officer (*principal financial officer*)	March 10, 2020
/s/Raymond Schinazi **Raymond Schinazi, PhD, DSc**	Director	March 10, 2020
/s/Shalini Sharp **Shalini Sharp**	Director	March 10, 2020
/s/Kevin Buehler **Kevin Buehler**	Director	March 10, 2020
/s/Tony Yao **Tony Yao, MD, PhD**	Director	March 10, 2020

Report of Independent Registered Public Accounting Firm

To the stockholders and the Board of Directors of Precision BioSciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Precision BioSciences, Inc. and subsidiaries (the "Company") as of December 31, 2019 and 2018, the related consolidated statements of operations, changes in stockholders' equity (deficit) and cash flows, for each of the two years in the period ended December 31, 2019, 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, 2019 and 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2019, in conformity with accounting principles generally accepted in the United States of America.

Change in Accounting Principle

As discussed in Note 1 to the financial statements, the Company has changed its method of accounting for revenue from contracts with customers in 2019 due to the adoption of Accounting Standards Update No. 2014-09, *Revenue from Contracts with Customers*.

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

Raleigh, North Carolina
March 9, 2020

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

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements.

PRECISION BIOSCIENCES, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 180,886	$ 103,193
Accounts receivable	965	523
Prepaid expenses	9,497	8,913
Other current assets	2,324	3,046
Total current assets	193,672	115,675
Property, equipment, and software—net	39,571	21,147
Intangible assets—net	1,432	1,466
Other assets	558	312
Total assets	$ 235,233	$ 138,600
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,037	$ 2,218
Accrued compensation	4,425	965
Accrued clinical and research and development expenses	2,400	1,569
Accrued other expenses and other current liabilities	1,584	887
Deferred revenue	16,486	8,436
Total current liabilities	26,932	14,075
Deferred revenue—noncurrent	65,895	82,807
Deferred rent—noncurrent	4,092	1,758
Total liabilities	96,919	98,640
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Series A convertible preferred stock; $0.0001 par value— no shares issued and outstanding as of December 31, 2019; 25,650,000 shares authorized, issued and outstanding as of December 31, 2018	—	3
Series B convertible preferred stock; $0.0001 par value— no shares issued and outstanding as of December 31, 2019; 21,956,100 shares authorized; 21,956,095 shares issued and outstanding as of December 31, 2018	—	2
Preferred stock, $0.0001 par value— 10,000,000 shares authorized as of December 31, 2019 and no shares authorized as of December 31, 2018; no shares issued and outstanding as of December 31, 2019	—	—
Common stock; $0.000005 par value— 200,000,000 shares authorized, 51,965,708 shares issued and 51,155,236 shares outstanding as of December 31, 2019; 16,717,117 shares issued and 15,906,645 shares outstanding as of December 31, 2018	—	—
Additional paid-in capital	316,333	126,094
Accumulated deficit	(177,067)	(85,187)
Treasury stock	(952)	(952)
Total stockholders' equity	138,314	39,960
Total liabilities and stockholders' equity	$ 235,233	$ 138,600

See notes to consolidated financial statements

PRECISION BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except share and per share amounts)

	For the Years Ended December 31, 2019	2018
Revenue	$ 22,238	$ 10,883
Operating expenses		
Research and development	82,416	45,122
General and administrative	27,026	13,673
Total operating expenses	109,442	58,795
Loss from operations	(87,204)	(47,912)
Other income (expense), net:		
Change in fair value of convertible notes payable	(9,758)	—
Interest expense	(182)	—
Interest income	4,267	1,875
Total other income (expense), net	(5,673)	1,875
Net loss and net loss attributable to common stockholders	$ (92,877)	$ (46,037)
Net loss per share attributable to common stockholders-basic and diluted	$ (2.21)	$ (2.92)
Weighted average shares of common stock outstanding-basic and diluted	41,991,162	15,775,541

See notes to consolidated financial statements

PRECISION BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except share amounts)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-In	Accumulated	Treasury	Total Stockholder's Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Deficit	Stock	(Deficit)
Balance- January 1, 2018	25,650,000	$ 3	—	$ —	16,496,801	$ —	$ 13,691	$ (39,111)	$ (952)	$ (26,369)
Issuance of Series B convertible preferred stock, net of issuance costs	—	—	21,956,095	2	—	—	109,740	—	—	109,742
Stock option exercises	—	—	—	—	220,316	—	171	—	—	171
Share-based compensation expense	—	—	—	—	—	—	2,492	(39)	—	2,453
Net loss	—	—	—	—	—	—	—	(46,037)	—	(46,037)
Balance- December 31, 2018	25,650,000	$ 3	21,956,095	$ 2	16,717,117	$ —	$ 126,094	$ (85,187)	$ (952)	$ 39,960
Adjustment to beginning accumulated deficit from adoption of ASU 2014-09	—	—	—	—	—	—	—	997	—	997
Conversion of convertible preferred stock into common stock upon initial public offering	(25,650,000)	(3)	(21,956,095)	(2)	22,301,190	—	5	—	—	—
Issuance of common stock upon conversion of convertible notes payable	—	—	—	—	2,921,461	—	49,490	—	—	49,490
Issuance of common stock in initial public offering, net of discounts and issuance costs	—	—	—	—	9,085,000	—	130,543	—	—	130,543
Stock option exercises	—	—	—	—	940,940	—	1,261	—	—	1,261
Share-based compensation expense	—	—	—	—	—	—	8,940	—	—	8,940
Net loss	—	—	—	—	—	—	—	(92,877)	—	(92,877)
Balance- December 31, 2019	—	$ —	—	$ —	51,965,708	$ —	$ 316,333	$ (177,067)	$ (952)	$ 138,314

See notes to consolidated financial statements

PRECISION BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	For the Years Ended December 31, 2019	2018
Cash flows from operating activities:		
Net loss	$ (92,877)	$ (46,037)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	5,317	2,354
Share-based compensation	8,940	2,453
Loss on disposal of property, equipment, and software	22	14
Non-cash interest expense	182	—
Change in fair value of convertible notes payable	9,758	—
Changes in operating assets and liabilities:		
Prepaid expenses	(584)	(7,476)
Accounts receivable	(441)	(523)
Other assets and other current assets	1,032	(448)
Accounts payable	667	(673)
Accrued other expenses and other current liabilities	4,835	1,790
Deferred revenue	(7,866)	(3,177)
Net cash used in operating activities	(71,015)	(51,723)
Cash flows from investing activities:		
Acquisition of license rights	—	(1,400)
Purchases of property, equipment and software	(24,666)	(14,278)
Proceeds from disposal of property, equipment, and software	—	15
Net cash used in investing activities	(24,666)	(15,663)
Cash flows from financing activities:		
Proceeds from stock option exercises	1,261	171
Issuance of Series B convertible preferred stock, net of issuance costs	—	109,742
Deferred offering costs	(2,622)	(2,136)
Issuance of convertible notes payable	39,550	—
Proceeds from IPO, net of underwriting discounts and commissions	135,185	—
Net cash provided by financing activities	173,374	107,777
Net increase in cash and cash equivalents	77,693	40,391
Cash and cash equivalents—beginning of period	103,193	62,802
Cash and cash equivalents —end of period	$ 180,886	$ 103,193
Supplemental disclosures of noncash financing and investing activities:		
Common stock issued on conversion of convertible notes payable	$ 49,490	$ —
Property, equipment and software additions included in accounts payable, accrued expenses and other current liabilities	$ 401	$ 1,340
Deferred offering costs included in accounts payable, accrued expenses and other current liabilities	$ 168	$ 406

See notes to consolidated financial statements

NOTE 1: DESCRIPTION OF BUSINESS AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Description of Business

Precision BioSciences, Inc. (the "Company") was incorporated on January 26, 2006 under the laws of the State of Delaware and is based in Durham, North Carolina. The Company is focused on utilizing its proprietary genome editing platform to help overcome cancers, cure genetic diseases and enable the development of safer, more productive food sources.

The Company's 100% owned subsidiary, Precision PlantSciences, Inc., was incorporated on January 4, 2012. Precision PlantSciences, Inc. amended its certificate of incorporation on January 16, 2018 to change its name to Elo Life Systems, Inc. Elo Life Systems Australia Pty Ltd was incorporated on May 29, 2018 as a 100% owned subsidiary of Elo Life Systems, Inc. The Company's 100% owned subsidiary, Precision BioSciences UK Limited, was incorporated on June 17, 2019. The accompanying consolidated financial statements include the accounts of the Company and its subsidiaries. Intercompany balances and transactions have been eliminated in consolidation.

Since its inception, the Company has devoted substantially all of its efforts to research and development activities, recruiting skilled personnel, developing manufacturing processes, establishing its intellectual property portfolio and providing general and administrative support for these operations. The Company is subject to a number of risks similar to those of other companies conducting high-risk, early-stage research and development of product candidates. Principal among these risks are dependence on key individuals and intellectual property, competition from other products and companies, and the technical risks associated with the successful research, development and clinical manufacturing of its product candidates. The Company's success is dependent upon its ability to continue to raise additional capital in order to fund ongoing research and development, obtain regulatory approval of its products, successfully commercialize its products, generate revenue, meet its obligations, and, ultimately, attain profitable operations.

On April 1, 2019, the Company completed its initial public offering ("IPO") in which the Company issued and sold 9,085,000 shares of its common stock at a public offering price of $16.00 per share and received approximately $130.5 million in net proceeds, after deducting underwriting discounts and commission of approximately $10.2 million and issuance costs of approximately $4.6 million.

In connection with the IPO, on March 15, 2019 the Company effected a reverse split of shares of the Company's common stock on a 1-for-2.134686 basis (the "Reverse Stock Split") of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for the Company's Series A and Series B preferred stock. Accordingly, all common shares, stock option shares, and per share amounts for all periods presented in the accompanying financial statements and notes thereto have been retroactively adjusted, where applicable, to reflect this Reverse Stock Split and adjustment of the preferred stock conversion ratios.

Authorized common shares were not affected by the Reverse Stock Split. Upon the closing of the IPO, all of the outstanding shares of convertible preferred stock automatically converted into 22,301,190 shares of common stock at the applicable ratio then in effect and the outstanding convertible notes payable, including accrued interest, were settled into 2,921,461 shares of common stock. Subsequent to the closing of the IPO, there were no shares of Series A or Series B convertible preferred stock or convertible notes payable outstanding.

Use of Estimates

The preparation of consolidated financial statements in conformity with accounting principles generally accepted in the United States of America ("GAAP") requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and disclosures made in the accompanying notes to the consolidated financial statements. Actual results could differ from those estimates. Significant estimates include recording revenue for performance obligations recognized over time, determination of the fair value of share-based compensation grants and estimating services expended by third-party service providers used to recognize research and development expense.

Basis of Presentation

These financial statements have been prepared in accordance with GAAP. Additionally, the accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. As of December 31, 2019, the Company has not generated any revenue from product sales and does not expect to generate any revenue from the sale of product in the foreseeable future. During the year ended December 31, 2019, the Company incurred a net loss of $92.9 million and, as of December 31, 2019, has an accumulated deficit of $177.1 million. The Company has financed operations primarily through its IPO, private placements of convertible preferred stock and convertible debt and with proceeds from its development and commercial license agreement with Les Laboratoires Servier, ("Servier") and Gilead Sciences, Inc. ("Gilead") (see Note 12). The Company expects to incur additional operating losses and negative operating cash flows for the foreseeable future.

Management believes that existing cash and cash equivalents will allow the Company to continue its operations into 2021. In the absence of a significant source of recurring revenue, the continued viability of the Company beyond that point is dependent on its ability to continue to raise additional capital to finance its operations. There can be no assurance that the Company will be able to obtain sufficient capital to cover its costs on acceptable terms, if at all.

Reclassifications

Certain reclassifications have been made to the presentation of amounts in our Consolidated Balance Sheet as of December 31, 2019 to conform to the prior year presentation. Specifically, certain current liabilities were reclassified from accrued expenses and other current liabilities and are now presented separately on our Consolidated Balance Sheets.

Summary of Significant Accounting Policies

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. As of December 31, 2019 and December 31, 2018, the Company held cash equivalents composed of money market funds and repurchase agreements that were collateralized by deposits in the form of government securities and obligations.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash and cash equivalents. All of the Company's cash and cash equivalents are held at financial institutions that management believes to be of high credit quality. The Company may maintain cash deposits in financial institutions in excess of government insured limits. The Company regularly invests excess cash deposits in money market funds and repurchase agreements. The Company believes that the credit risk arising from the holdings of these financial instruments is mitigated by the fact that these securities are of short duration, government backed and of high credit rating. The Company has not experienced any losses on cash and cash equivalents to date.

Revenue from two development and license agreements accounted for 60% and 33% of revenue during 2019 and 34% and 53% of revenue during 2018, as well as 2% and 98% of deferred revenue as of December 31, 2019.

Deferred Equity Offering Costs

The Company capitalizes incremental legal, professional accounting and other third-party fees directly associated with the Company's planned equity offerings as other current assets until the equity offering is consummated. After consummation, these costs are recorded in stockholders' equity (deficit) as a reduction of additional paid-in capital. If the equity offering is not completed, any costs deferred will be expensed immediately.

Property, Equipment and Software

Property, equipment and software are stated at cost, net of depreciation and amortization. Depreciation and amortization are calculated using the straight-line method over the estimated useful lives of the assets ranging from three to seven years. Leasehold improvements are amortized on a straight-line basis over the shorter of the lease term or estimated useful life of the asset.

The depreciation and amortization periods for the Company's significant property, equipment and software categories are as follows:

Computer hardware and software	3 years
Lab equipment	5 to 7 years
Furniture and office equipment	3 to 5 years
Leasehold improvements	Lesser of remaining lease term or useful life

Repairs and maintenance are charged to operations as incurred, and expenditures for additions and improvements that extend the useful life of the asset are capitalized.

Intangible Assets

Intangible assets primarily include licenses and patents. The Company capitalizes license fees paid to acquire access to proprietary technology if the technology is expected to have alternative future use in multiple research and development projects. The cost of licensed technology rights is amortized using the straight-line method over the estimated useful life of the technology. If the access to use the technology rights is one year or less, the cost is recorded as a prepaid expense and amortized over the period identified in the agreement. Amortization expense for licensed technology and capitalized patent costs is included in research and development expenses within the accompanying consolidated statement of operations.

Impairment of Long-Lived Assets

Long-lived assets, such as property, equipment and software and intangible assets, subject to amortization, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. An impairment loss is assessed when future undiscounted cash flows are less than the assets' carrying value and recognized when the carrying value of the asset exceeds fair value. Fair value is calculated by estimating the discounted future cash flows expected to be generated by the asset as well as other valuation techniques. An impairment charge is recognized for the amount by which the carrying amount exceeds the fair value of the asset.

Revenue Recognition for Contracts with Customers

The Company's revenues are generated primarily through collaborative research, license, development and commercialization agreements.

Effective January 1, 2019, the Company adopted Accounting Standards Update ("ASU") No. 2014-09, *Revenue from Contracts with Customers* ("ASC 606"), using the modified retrospective transition method. Under this method, results for reporting periods beginning on January 1, 2019 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC Topic 605, *Revenue Recognition* ("ASC 605"). The Company applied the modified retrospective transition method to contracts that were not completed as of January 1, 2019. For the year ended December 31, 2019, the Company reduced revenue recognition by $1.4 million for changes in total estimated time to be incurred in the future to satisfy the performance obligation. ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation.

At contract inception, once the contract is determined to be within the scope of ASC 606, the Company evaluates the performance obligations promised in the contract that are based on goods and services that will be transferred to the customer and determines whether those obligations are both (i) capable of being distinct and (ii) distinct in the context of the contract. Goods or services that meet these criteria are considered distinct performance obligations. If both these criteria are not met, the goods and services are combined into a single performance obligation. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, these options are considered performance obligations. The exercise of a material right is accounted for as a contract modification for accounting purposes.

The Company recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is based on the use of an output or input method.

Amounts received prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue within current liabilities in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue – noncurrent. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets in the other current assets line item in the accompanying consolidated balance sheets.

Milestone Payments – If an arrangement includes development and regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price 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. Milestone payments that are not within the Company's or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received and therefore revenue recognized is constrained as management is unable to assert that a reversal of revenue would not be possible. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues and earnings in the period of adjustment.

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

Significant Financing Component – In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. The Company assessed each of its revenue arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in any of its arrangements.

Collaborative Arrangements – The Company has entered into collaboration agreements, which are within the scope of ASC 606, to discover, develop, manufacture and commercialize product candidates. The terms of these agreements typically contain multiple promises or obligations, which may include: (1) licenses, or options to obtain licenses, to use the Company's technology, (2) research and development activities to be performed on behalf of the collaboration partner, and (3) in certain cases, services in connection with the manufacturing of preclinical and clinical material. Payments the Company receives under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; clinical and development, regulatory, and sales milestone payments; and royalties on future product sales.

The Company analyzes its collaboration arrangements to assess whether the collaboration agreements are within the scope of accounting standards codification ("ASC") ASC 808, *Collaborative Arrangements* ("ASC 808") to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and, therefore, are within the scope of ASC 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to ASC 606. For those elements of the arrangement that are accounted for pursuant to ASC 606, the Company applies the five-step model described above.

For additional discussion of accounting for collaboration revenues, see Note 12, "Collaboration and license agreements."

Research and Development

Research and development costs are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities including salaries, benefits, share-based compensation, allocations for rent and facility costs, depreciation, preclinical manufacturing expenses, costs of services provided by contract research organizations ("CROs") in connection with preclinical trials and contract manufacturing organizations ("CMOs") engaged to manufacture clinical trial material, costs of licensing technology, and costs of services provided by research organizations and service providers. Upfront payments and milestone payments made for the licensing of technology are expensed as research and development in the period in which they are incurred if the technology is not expected to have any alternative future uses other than the specific research and development project for which it was intended. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed rather than when the payment is made.

The Company is required to estimate accrued research and development expenses resulting from its obligations under contracts with CROs, CMOs, research organizations, service providers, vendors and consultants in connection with research and development activities. The financial terms of these contracts are subject to negotiations and vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to the Company under such contracts. The Company's objective is to reflect the appropriate research and development expenses in its consolidated financial statements by matching those expenses with the period in which the services and efforts are expended. There may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the Company's estimate, the Company adjusts the accrual or amount of prepaid expense accordingly.

Although the Company does not expect its estimates to be materially different from amounts actually incurred, the Company's understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in the Company reporting amounts that are too high or too low in any particular period. To date, the Company has not made any material adjustments to prior estimates of accrued research and development expenses.

Common Stock Valuation

Prior to the IPO, due to the absence of an active market for the Company's common stock, the Company utilized methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, Valuation of Privately-Held Company Equity Securities Issued as Compensation, to estimate the fair value of its common stock. In determining the exercise prices for stock options granted prior to the IPO, the Company considered the estimated fair value of the common stock as of the measurement date. The estimated fair value of the common stock was determined based upon a variety of factors, including the illiquid nature of the common stock, the Company's financial position and historical financial performance, the status of technological developments within the Company's research, the composition and ability of the current research and management team, an evaluation or benchmark of the Company's competition and the current business climate in the marketplace. Significant changes to the key assumptions underlying the factors used could result in different fair values of common stock at each valuation date.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2019 and December 31, 2018, there was no difference between net loss and comprehensive loss in the accompanying consolidated financial statements.

Net Loss Per Share

Basic net loss per share is computed by dividing net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is computed using the weighted-average number of shares of common stock outstanding during the period and, if dilutive, the weighted-average number of potential shares of common stock. Diluted net loss per share is the same as basic net loss per share for the years ended December 31, 2019 and December 31, 2018 since all potential shares of common stock are anti-dilutive as a result of the net loss.

Share-Based Compensation

The Company accounts for all share-based compensation, including stock options and the employee stock purchase plan at fair value and recognizes compensation expense for those equity awards, net of actual forfeitures, over the requisite service period, which is generally the vesting period of the respective award.

The fair value of each equity grant is estimated on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of the Company's common stock and assumptions the Company makes for the volatility of its common stock, the expected term of the stock options, the risk-free interest rate for a period that approximates the expected term of the stock options and the Company's expected dividend yield. As the Company has limited trading history, expected volatility is estimated based on the historical volatility of publicly traded peer companies and the Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of our traded share price. The expected term of the options has been determined utilizing a weighted value considering actual history and estimated expected term based on the midpoint of final vest date and expiration date. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

Income Taxes

Deferred tax assets and liabilities are determined based on the temporary differences between the consolidated financial statement carrying amounts and the tax basis of assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. In estimating future tax consequences, all expected future events are considered other than the enactment of changes in the tax law or rates. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes.

The Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities based on the technical merits of the position. The tax benefits recognized in the consolidated financial statements from such a position is measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate settlement.

The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

Accounting Standards Updates

The Company is an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may take advantage of reduced reporting requirements that are otherwise applicable to public companies. Section 107 of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies are required to comply with those standards. The Company has elected to use the extended transition period for complying with new or revised accounting standards. The JOBS Act also exempts the Company from having to provide an auditor attestation of internal controls over financial reporting under Sarbanes-Oxley Act Section 404(b).

The Company will remain an "emerging growth company" until the earliest of (i) December 31, 2024, (ii) the last day of the fiscal year in which it has total annual gross revenues of $1.07 billion or more, (iii) the date on which it has issued more than $1.0 billion in nonconvertible debt during the previous three years or (iv) the date on which it is deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission ("SEC"), which generally is when it has more than $700 million in market value of its stock held by non-affiliates, has been a public company for at least 12 months and have filed one annual report on Form 10-K.

In May 2014, the Financial Accounting Standards Board, or FASB, issued ASC 606, which superseded the revenue requirements in ASC 605. In 2015 and 2016, the FASB issued additional ASUs related to ASC 606 that delayed the effective date of the guidance and clarified various aspects of the new revenue guidance, including principal versus agent considerations, identifying performance obligations, and licensing, and they include other improvements and practical expedients. Effective January 1, 2019, the Company adopted ASC 606 using the modified retrospective transition method.

As a result of adopting ASC 606, the Company recorded a $1.0 million transition adjustment in the first quarter of 2019 to reduce the opening balance of accumulated deficit as of January 1, 2019 primarily as a result of the treatment of the up-front consideration received from the Company's collaboration agreements under prior revenue recognition guidance.

A summary of the amount by which each financial statement line item was affected by the impact of the cumulative adjustment is set forth in the table below:

	Impact of ASC 606 Adoption on Consolidated Balance Sheet as of January 1, 2019		
(in thousands)	As reported under ASC 606	Adjustments	Balances without adoption of ASC 606
Deferred revenue - current liabilities	$ 8,029	$ 407	$ 8,436
Deferred revenue - noncurrent liabilities	82,217	590	82,807
Accumulated deficit	(84,190)	(997)	(85,187)

A summary of the amount by which each financial statement line item was affected in the current reporting period by ASC 606 as compared with the guidance that was in effect prior to adoption is set forth in the tables below:

	Impact of ASC 606 Adoption on Consolidated Balance Sheet as of December 31, 2019		
(in thousands)	As reported under ASC 606	Adjustments	Balances without adoption of ASC 606
Deferred revenue - current liabilities	$ 16,486	$ (8,017)	$ 8,469
Deferred revenue - noncurrent liabilities	65,895	11,427	77,322
Accumulated deficit	(177,067)	(3,410)	(180,477)

	Impact of ASC 606 Adoption on Consolidated Statement of Operations for the Years Ended December 31, 2019		
(in thousands, except per share data)	As reported under ASC 606	Adjustments	Balances without adoption of ASC 606
Revenue	$ 22,238	$ (2,413)	$ 19,825
Net loss	(92,877)	(2,413)	(95,290)
Net loss per share - basic and diluted	(2.21)	(0.06)	(2.27)

	Impact of ASC 606 Adoption on Consolidated Statement of Cash Flows for the Years Ended December 31, 2019		
(in thousands)	As reported under ASC 606	Adjustments	Balances without adoption of ASC 606
Net loss	$ (92,877)	$ (2,413)	$ (95,290)
Changes in deferred revenue	(7,866)	2,413	(5,453)

During the year ended December 31, 2019, the Company recorded $9.4 million in revenue that was included in deferred revenue as of December 31, 2018. The most significant change to the Company's revenue recognition as a result of the adoption of ASC 606 relates to the accounting for certain option fees and milestone payments in determining the transaction price (step (iii)), and the revenue recognition pattern (step (v)) related to the Company's development and commercial license agreement with Servier. Under ASC 605, the option fees payable by the Company to exercise the 50/50 co-development and co-promotion option was accounted for as a reduction in the arrangement consideration, and certain development milestones that may be earned for early-stage pre-IND development milestones were included in the arrangement consideration as the early-stage pre-IND development milestones were deemed to be non-substantive. Under ASC 606, the option fees were not accounted for as a reduction in the transaction price as the option fees are contingent upon Servier's exercise of its commercial (customer) options on licensed product candidates, and the milestone payments were excluded from the transaction price based on the assessment of the most likely amount and application of the variable consideration constraint, since the milestones relate to successful achievement of certain developmental goals, which may not be achieved. In addition, under ASC 605, the Company recognized revenue on a straight-line basis over the period the Company expected to complete its obligations. Under ASC 606, the Company recognizes revenue based on the proportional performance of the services related to the performance obligation expected. For further discussion of the adoption of ASC 606 see Note 12, "Collaboration and license agreements."

In June 2018, the FASB issued ASU 2018-07, *Compensation-Stock Compensation Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"). ASU 2018-07 substantially aligns accounting for share-based payments to employees and non-employees. This ASU became effective for annual periods beginning after December 15, 2018 including interim periods within that period, and early adoption is permitted. The Company adopted ASU 2018-07 effective January 1, 2019. The adoption of the standard did not have a material impact on the Company's consolidated financial statements.

In August 2018, the FASB issued ASU 2018-13, *Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"). ASU 2018-13 is intended to improve the effectiveness of disclosures in the notes to financial statements related to fair value measurements in Topic 820. This ASU will become effective for annual periods beginning after December 15, 2019, including interim periods within that period, and early adoption is permitted. The adoption of this standard is not expected to have a material impact on the Company's consolidated financial statements and related disclosures.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808)—Clarifying the Interaction between Topic 808 and ASC 606* ("ASU 2018-18"). The amendments in ASU 2018-18 make targeted improvements to GAAP for collaborative arrangements by clarifying that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606 when the collaborative arrangement participant is a customer in the context of a unit of account. In those situations, all the guidance in ASC 606 should be applied, including recognition, measurement, presentation, and disclosure requirements. In addition, unit-of-account guidance in ASU 2018-18 was aligned with the guidance in ASC 606 (that is, a distinct good or service) when an entity is assessing whether the collaborative arrangement or a part of the arrangement is within the scope of ASC 606. ASU 2018-18 is effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption is permitted, including adoption in any interim period. The amendments should be applied retrospectively to the date of initial application of ASC 606. The Company adopted this guidance effective January 1, 2019 with its initial application of ASC 606. The adoption of the standard did not have an impact on the Company's consolidated financial statements.

In November 2019, the FASB issued ASU 2019-10, *Financial Instruments — Credit losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842)* ("ASU 2019-10"), which provides a one-year deferral of the effective dates of ASU No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), issued in February 2016. ASU 2016-02 was issued in order to improve comparability among organizations by recognizing lease assets and liabilities in the consolidated balance sheets for those leases previously classified as operating leases under GAAP. The update requires a lessee to recognize in its consolidated balance sheet a liability to make lease payments and also a right-of-use asset representing its right to use the underlying asset for the lease term. ASU 2019-10 is effective for fiscal years beginning after December 15, 2020 and interim periods within fiscal years beginning after December 15, 2021. The Company is currently evaluating the impact that this standard will have on its consolidated financial statements and expects to have an increase in total assets and total liabilities as a result of adopting the lease standard.

Other accounting standards updates issued, but not effective until after December 31, 2019, are not expected to have a material effect on the Company's consolidated financial position, statements of operations or cash flows.

NOTE 2: PROPERTY, EQUIPMENT AND SOFTWARE

Property, equipment and software consisted of the following as of December 31 (in thousands):

	2019	2018
Construction in progress	$ 697	$ 8,600
Leasehold improvements	25,969	5,733
Software	328	278
Laboratory equipment	19,251	10,057
Office equipment	1,602	839
Furniture and fixtures	2,373	1,124
Total property, equipment and software	50,220	26,631
Less accumulated depreciation and amortization	10,649	5,484
Property, equipment and software - net	$ 39,571	$ 21,147

In July 2019, we completed construction and opened our Manufacturing Center for Advanced Therapeutics, or MCAT, a manufacturing facility supporting our therapeutic product development platform, in a leased facility in Research Triangle Park. Of the $8.6 million construction-in-progress (CIP) balance as of December 31, 2018, $2.5 million related to the MCAT and $4.4 million related to our other leased facilities in Durham was recognized as leasehold improvements in the year ending December 31, 2019.

Depreciation expense, including amortization of leasehold improvements and software, was $5.3 million and $2.3 million for the years ended December 31, 2019 and December 31, 2018, respectively.

NOTE 3: INTANGIBLE ASSETS

Intangible assets, net, consisted of the following as of December 31 (in thousands):

	2019	2018
License cost	$ 1,831	$ 1,831
Less: accumulated amortization	(281)	(247)
Less: impairments	(118)	(118)
Intangible assets, net	1,432	1,466

Amortization expense of the intangible assets was $0.1 million for the years ended December 31, 2019 and December 31, 2018.

In September 2018, the Company entered into a license agreement to obtain the rights to intellectual property for the production of biological materials for use in its development programs. The Company paid the licensor a one-time, non-refundable license fee of $1.4 million for rights to a cell line that can be used on up to four product candidates. The intellectual property rights are being amortized on a straight-line basis over a period of 216 to 257 months depending on the date the company adds product candidates to the agreement. Amortization expense will be approximately $0.1 million for each of the next five years with the remaining $0.9 million amortized to expense in 2025 and beyond.

NOTE 4: STOCKHOLDERS' EQUITY

Capital Structure

Upon the closing of the IPO, all of the Company's outstanding shares of the Series A and Series B convertible preferred stock automatically converted into 22,301,190 shares of common stock and the Company's outstanding convertible notes payable, including accrued interest, converted into 2,921,461 shares of common stock at the applicable conversion ratio. Subsequent to the closing of the IPO, there were no shares of preferred stock outstanding.

On April 1, 2019, the Company filed an amendment to its amended and restated certificate of incorporation pursuant to which, among other things, the Company increased its authorized shares to 210,000,000 shares of capital stock, of which 200,000,000 shares were designated as $0.000005 par value common stock and 10,000,000 shares were designated as $0.0001 par value preferred stock.

NOTE 5: SHARE-BASED COMPENSATION

Under the terms of its equity incentive award plans, the Company's board of directors may grant equity or equity-based awards to employees, directors and other service providers. The Company granted stock options under the 2006 Stock Incentive Plan ("2006 Plan") until April 2015 when the 2015 Stock Incentive Plan ("2015 Plan") was adopted. The 2006 Plan expired in 2016 and there are no remaining shares available to be granted under the 2006 Plan. There were 1,385,203 stock options outstanding under the 2006 Plan as of December 31, 2019.

Upon adoption of the 2015 Plan, there were 5,270,095 shares of common stock reserved for issuance. In May 2018, the Company amended the 2015 Plan to increase the number of shares reserved for issuance to 8,211,980. The 2015 Plan had 5,462,954 stock options outstanding as of December 31, 2019. The Company's board of directors determined the terms of stock options granted under the 2015 Plan, including option exercise prices and vesting.

On March 12, 2019, the Company's board of directors adopted, and, on or about March 14, 2019 the Company's stockholders approved, the Precision BioSciences, Inc. 2019 Incentive Award Plan ("2019 Plan") and the 2019 Employee Stock Purchase Plan ("2019 ESPP"), both of which became effective on March 27, 2019. On March 27, 2019, the Company ceased granting new awards under the 2015 Plan.

The 2019 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock, restricted stock units and other share-based awards initially equal to 4,750,000 shares of common stock. The 2019 Plan provides for an annual increase to the number of shares of common stock available for issuance on the first day of each calendar year beginning January 1, 2020 and ending on and including January 1, 2029 by an amount equal to the lesser of (i) 4% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as determined by the board of directors. The number of shares available for issuance under the 2019 Plan was increased by 2,046,209 on January 1, 2020 pursuant to this provision. Any shares that are subject to awards outstanding under the Company's 2006 Plan and 2015 Plan as of the effective date of the 2019 Plan that expire, lapse, or are terminated, exchanged for cash, surrendered, repurchased, or canceled without having been fully exercised or forfeited, to the extent so unused, will become available for award grants under the 2019 Plan. The 2019 Plan had 2,070,959 stock options outstanding as of December 31, 2019.

Up to 525,000 shares of the Company's common stock were initially reserved for issuance under the 2019 ESPP. The 2019 ESPP provides for an annual increase to the number of shares available for issuance on the first day of each calendar year beginning January 1, 2020 and ending on and including January 1, 2029 by an amount equal to the lesser of (i) 1% of the shares outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares as is determined by our board of directors. The number of shares available for issuance under the 2019 ESPP was increased by 511,552 shares on January 1, 2020 pursuant to this provision. No more than 5,250,000 shares of our common stock may be issued under our 2019 ESPP. The purchase price of the shares, in the absence of a contrary designation, will be 85% of the lower of the fair market value of our common stock on the first trading day of the offering period or on the purchase date. The first ESPP offering period commenced on October 21, 2019 and ended on February 29, 2020; 44,197 shares were issued with respect to this offering period. The next ESPP offering period commenced on March 1, 2020 and will end on August 31, 2020.

The Company recorded employee and nonemployee share-based compensation expense as follows (in thousands):

	Years Ended December 31,	
	2019	2018
Employee	$ 8,354	$ 2,431
Nonemployee	586	22
	$ 8,940	$ 2,453

Share-based compensation expense related to stock options is included in the following line items in the consolidated statements of operations (in thousands):

	Years Ended December 31,	
	2019	2018
Research and development	$ 5,639	$ 1,817
General and administrative	3,301	636
	$ 8,940	$ 2,453

Determining the appropriate fair value model to measure the fair value of the stock option grants on the date of grant and the related assumptions requires judgment. The fair value of each stock option grant is estimated using a Black-Scholes option-pricing model on the date of grant as follows:

	Years Ended December 31,	
	2019	2018
Estimated dividend yield	0.00%	0.00%
Weighted-average expected stock price volatility	68.25%	68.44%
Weighted-average risk-free interest rate	1.98%	2.95%
Expected term of options (in years)	6.61	6.01
Weighted-average fair value per option	$ 7.62	$ 7.37

The expected volatility rates are estimated based on the actual volatility of comparable public companies over the expected term. The expected term represents the average time that stock options that vest are expected to be outstanding. The Company does not have sufficient history of exercising stock options to estimate the expected term of employee stock options and thus utilizes a weighted value considering actual history and estimated expected term based on the midpoint of final vest date and expiration date. The risk-free rate is based on the United States Treasury yield curve during the expected life of the option.

The following table summarizes activity in the Company's stock option plans for the years ended December 31, 2019 and December 31, 2018:

	Outstanding Option Shares	Weighted-Average Exercise Price
Balance as of January 1, 2018	5,416,025	$ 0.62
Granted	3,160,097	11.66
Exercised	(220,308)	0.78
Forfeited/canceled	(592,350)	2.01
Balance as of December 31, 2018	7,763,464	5.00
Granted	2,647,236	11.64
Exercised	(940,940)	1.34
Forfeited/canceled	(550,644)	10.47
Balance as of December 31, 2019	8,919,116	7.02

The intrinsic value of stock options exercised was $10.6 million and $2.7 million during the years ended December 31, 2019 and December 31, 2018, respectively.

There was approximately $29.0 million of total unrecognized compensation cost related to unvested stock options as of December 31, 2019, which is expected to be recognized over a weighted-average period of 2.9 years.

The following table summarizes certain information about stock options granted under the stock option plans which are vested or expected to vest as of December 31, 2019 and December 31, 2018.

Years Ended December 31,		Number of Options	Weighted-Average Remaining Contractual Life (in years)	Weighted-Average Exercise Price
2019	Expected to be exercisable	8,919,116	7.19	$ 7.02
2019	Currently exercisable	4,082,663	5.08	$ 3.12
2018	Expected to be exercisable	7,763,464	7.50	$ 5.00
2018	Currently exercisable	3,418,993	5.37	$ 0.76

The following table summarizes certain information about stock options outstanding under the stock option plans for the years ending December 31, 2019 and December 31, 2018, respectively:

Year Ended December 31, 2019			
Exercise price	Number of Options Outstanding	Weighted- Average Remaining Life	Number of Options Exercisable
$0.01 - $0.04	1,385,203	1.50	1,385,203
$0.41 - $1.20	2,310,993	6.32	1,721,811
$7.74 - $9.46	1,266,454	9.44	131,644
$10.17 - $13.80	3,891,922	8.96	844,005
$14.91 - $16.00	64,544	9.59	—
	8,919,116		4,082,663

Year Ended December 31, 2018			
Exercise price	Number of Options Outstanding	Weighted- Average Remaining Life	Number of Options Exercisable
$0.01 - $0.04	1,397,203	2.49	1,397,203
$0.41	1,440,920	6.65	1,166,591
$1.18 - $1.20	1,846,255	8.24	748,922
$8.99	291,023	9.30	33,376
$10.17	289,408	9.56	5,708
$11.98	2,070,029	9.78	67,193
$13.20	428,626	9.93	—
	7,763,464		3,418,993

NOTE 6: RETIREMENT PLAN

In January 2011, the Company established a defined contribution 401(k) retirement savings plan (the "Retirement Plan") to all full-time employees. Employee contributions to the Retirement Plan can be 100% of annual compensation up to the prescribed annual maximum under the Internal Revenue Code. Administrative fees of less than $0.1 million were paid by the Company for the years ended December 31, 2019 and December 31, 2018.

The Retirement Plan includes a safe-harbor matching employer contribution equal to 100% of participants' deferral contributions up to 4%. The Company made contributions of $0.6 million and $0.4 million to the Retirement Plan during the years ended December 31, 2019 and December 31, 2018, respectively.

NOTE 7: COMMITMENTS AND CONTINGENCIES

Litigation

The Company is subject to various legal matters and claims in the ordinary course of business. Although the results of legal proceedings and claims cannot be predicted with certainty, in the opinion of management, there are currently no such known matters that will have a material effect on the consolidated financial condition, results of operations or cash flows of the Company.

Leases

The Company leases office and laboratory space under long-term operating leases. These leases provide tenant improvement allowances and rent abatements as incentives for the Company to either enter into the initial lease agreement or expand within existing premises already under lease and represent all of the Company's lease obligations as of December 31, 2019. These leases include the following:

- Office and laboratory space at 302 East Pettigrew Street, Durham, North Carolina, which is the Company's corporate headquarters. The property is leased through July 2024 with the option to extend.
- Laboratory and office space at 3054 Cornwallis Road Durham, North Carolina. The property is leased through April 2026 with the option to extend.
- Laboratory space at 20 TW Alexander Drive, Research Triangle Park, North Carolina. In December 2019, the Company expanded the amount of spaced leased at this site and extended to lease to August 2027.

The following is a schedule of future minimum lease payments for all leases as of December 31, 2019 (in thousands):

	Operating Leases
2020	2,706
2021	3,099
2022	3,196
2023	3,288
2024	2,611
2025 and beyond	3,066
Total	17,966

Supply Agreements

The Company enters into contracts in the normal course of business with CMOs for the manufacture of clinical trial materials and CROs for clinical trial services. These agreements provide for termination at the request of either party with less than one-year notice and are, therefore, cancelable contracts and, if canceled, are not anticipated to have a material effect on the consolidated financial condition, results of operations, or cash flows of the Company.

NOTE 8: NET LOSS PER SHARE

The Company's potential dilutive securities have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of shares of common stock outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same.

The Company excluded the following potential shares of common stock from the computation of diluted net loss per share attributable to common stockholders because including them would have had an anti-dilutive effect:

	Years Ended December 31,	
	2019	2018
Series A preferred stock (as converted to common stock)	—	12,015,814
Series B preferred stock (as converted to common stock)	—	10,285,376
Outstanding share-based compensation awards converted to common stock	4,032,359	4,796,377
Total	4,032,359	27,097,567

NOTE 9: DEBT

In March 2019, the Company entered into a note purchase agreement pursuant to which it sold and issued an aggregate of $39.6 million of convertible notes payable (the "2019 Notes").

The 2019 Notes accrued interest at a rate of 6% per annum. The 2019 Notes were settled in 2,921,461 shares of common stock in connection with the closing of the Company's IPO (see Note 1) at a settlement price of $13.60 per share (equal to 85% of the IPO price per share).

On issuance, the Company elected to account for the 2019 Notes at fair value with any changes in fair value being recognized through the consolidated statements of operations until the 2019 Notes were settled. The fair value of the 2019 Notes was determined to be $39.6 million on issuance and $49.4 million as of April 1, 2019, the settlement date. For the year ended December 31, 2019, the Company recognized $9.8 million of expense as changes in fair value and $0.2 million of interest expense.

Revolving Line

In May 2019, the Company entered into a loan and security agreement with Pacific Western Bank (the "Pacific Western Loan Agreement") pursuant to which the Company may request advances on a revolving line of credit of up to an aggregate principal of $50.0 million (the "Revolving Line"). The maturity date of the Revolving Line is May 15, 2022.

The Revolving Line bears interest at an annual rate equal to the greater of (i) 1.25% below the prime rate then in effect, or (ii) 4.25% at all times when the Company maintains a daily balance of cash in its demand deposit accounts at Pacific Western Bank of at least $25.0 million, and the greater of (i) 0.25% above the prime rate then in effect; or (ii) 5.75% at all times when the Company does not maintain a daily balance of cash in demand deposit accounts at Pacific Western Bank of at least $25.0 million. The Pacific Western Loan Agreement requires that the Company pay a quarterly fee in an amount equal to 0.50% per annum of the unused portion of the Revolving Line. The unused fee shall be waived for any quarter the Company maintains a daily balance in its demand deposit accounts of at least $25.0 million. If the Revolving Line is terminated prior to the maturity date, the Company is required to pay an early termination fee equal to 1.0% of the Revolving Line.

The Company granted Pacific Western Bank a security interest in substantially all of its assets, excluding any of the intellectual property now or hereafter owned, but including any rights to payment from the sale or licensing of any such intellectual property. The Company is prohibited from paying cash dividends without the prior written consent of Pacific Western Bank. The Pacific Western Loan Agreement includes customary representations, warranties and covenants (affirmative and negative) and was amended in December 2019 to allow the Company to maintain a bank account with a non-affiliated bank in the United Kingdom provided that the account balance does not exceed 1.5 million GBP or its U.S. dollar equivalent at any time.

There were no borrowings, and the Company was in compliance with its financial covenants, under the Pacific Western Loan Agreement as of December 31, 2019.

NOTE 10: INCOME TAXES

The Company recorded no income tax expense due to the operating losses incurred for the years ended December 31, 2019 and December 31, 2018.

Significant components of the Company's deferred tax assets and deferred tax liabilities are as follows (in thousands):

	Years Ended December 31,	
	2019	2018
Noncurrent deferred tax assets:		
Net operating loss carryforwards	$ 23,358	$ 9,185
Contribution carryforwards	34	29
Deferred rent	1,099	449
Deferred revenue	13,172	9,454
Other assets	2,444	573
Tax credits	9,090	3,632
Less: valuation allowance	(47,734)	(22,736)
Total deferred tax assets, noncurrent	1,463	586
Noncurrent deferred tax liability:		
Property and equipment	1,463	586
Total deferred tax liabilities, noncurrent	1,463	586
Net deferred tax assets	$ —	$ —

As of December 31, 2019 and December 31, 2018, the Company has provided a valuation allowance for the full amount of the net deferred tax assets as the realization of the net deferred tax assets is not determined to be more likely than not. The net increase in the valuation allowance for the year ended December 31, 2019 of $25.0 million is comprised of an increase in deferred tax assets, primarily related to deferred revenue and net operating loss carryforwards, for the year.

The reasons for the difference between actual income tax benefit for the years ended December 31, 2019 and December 31, 2018 and the amount computed by applying the statutory federal income tax rate to losses before income tax benefit are as follows (in thousands):

	Year Ended December 31, 2019		Year Ended December 31, 2018	
	Amount	% of Pre-Tax Earnings	Amount	% of Pre-Tax Earnings
Income tax expense at statutory rate	$ (19,505)	21.0%	$ (9,668)	21.0%
State income taxes, net of federal tax benefit	(1,827)	2.0%	(909)	2.0%
Non-deductible expenses	1,784	(1.9%)	270	(0.6%)
R&D and orphan drug credits	(4,810)	5.1%	(1,934)	4.2%
Other	(639)	0.7%	(31)	0.1%
Change in valuation allowance	24,997	(26.9%)	12,272	(26.7%)
Income tax (benefit) expense	$ —	—	$ —	—

As of December 31, 2019, the Company had federal, state, and foreign net operating loss ("NOL") carryforwards of approximately $101.3 million, $101.7 million, and $0.4 million respectively. At December 31, 2018, the Company had federal and state NOL carryforwards of approximately $40 million and $39.8 million, respectively. Federal NOL carryforwards of $19.7 million begin to expire in 2030 while the remaining federal NOL carryforward of $81.6 million carries forward indefinitely. The state NOL carryforwards begin to expire in 2025. The foreign NOLs carryforward indefinitely. At December 31, 2019, the Company had federal and state research and development ("R&D") tax credits of $7.2 million and an amount less than $0.1 million, which begin to expire in 2027 and 2030, respectively. At December 31, 2018, the Company had federal and state tax R&D credits of $3.6 million and an amount less than $0.1 million which begin to expire in 2027 and 2030, respectively. At December 31, 2019 and December 31, 2018, the Company had federal Orphan Drug credits of $1.8 million and $0.7 million, respectively, which begin to expire in 2038. At December 31, 2019 and December 31, 2018, the Company had federal contribution carryforwards of $0.1 million and an amount less than $0.1 million, respectively, which begin to expire in 2020.

The Company incorporated a subsidiary in Australia in 2018. However, the subsidiary has had minimal losses since inception. As such, there are no undistributed earnings as of December 31, 2019. The Company incorporated a subsidiary in the United Kingdom in 2019. However, the subsidiary has had minimal activity since inception. As such, there are no undistributed earnings as of December 31, 2019.

The Company's ability to utilize its NOL and R&D credit carryforwards may be substantially limited due to ownership changes that may have occurred or that could occur in the future, as required by Section 382 of the Internal Revenue Code of 1986, as amended (the Code), as well as similar state provisions. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change," as defined by Section 382 of the Code, results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percent of the outstanding stock of a company by certain stockholders or public groups. The Company has not completed a study to assess whether one or more ownership changes have occurred since the Company became a loss corporation under the definition of Section 382. If the Company has experienced an ownership change, utilization of the NOL or R&D credit carryforwards would be subject to an annual limitation, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term, tax-exempt rate, and then could be subject to additional adjustments, as required. Any such limitation may result in the expiration of a portion of the NOL or R&D credit carryforwards before utilization. Until a study is completed and any limitation known, no amounts are being considered as an uncertain tax position or disclosed as an unrecognized tax benefit. Any carryforwards that expire prior to utilization as a result of such limitations will be removed from deferred tax assets with a corresponding reduction of the valuation allowance. Due to the existence of the valuation allowance, it is not expected that any possible limitation will have an impact on the results of operations of the Company.

The Company reflects in the accompanying consolidated financial statements the benefit of positions taken in a previously filed tax return or expected to be taken in a future tax return only if it is considered 'more-likely-than-not' that the position taken will be sustained by the appropriate taxing authority. As of December 31, 2019 and December 31, 2018, the Company had no unrecognized income tax benefits. The Company's policy for recording interest and penalties relating to uncertain income tax positions is to record them as a component of income tax expense in the accompanying consolidated statements of operations. As of December 31, 2019 and December 31, 2018, the Company had no such accruals.

The Tax Cuts and Jobs Act of 2017 subjects a U.S. shareholder to tax on global intangible low-taxed income ("GILTI") earned by certain foreign subsidiaries. The FASB Staff Q&A, Topic 740, No. 5, Accounting for Global Intangible Low-Taxed Income, states that an entity can make an accounting policy election to either recognized deferred taxes for temporary basis differences expected to reverse as GILTI in future years or to provide for the tax expense related to GILTI in the year the tax is incurred as a period expense only. The Company has elected to account for GILTI in the year the tax is incurred. The Company does not have a GILTI inclusion in years ends December 31, 2019 or December 31, 2018 and therefore, no GILTI tax has been recorded for the years then ended.

NOTE 11: FAIR VALUE MEASUREMENTS

The carrying amounts of the Company's financial instruments, including accounts receivable, accounts payable, and accrued expenses and other current liabilities, approximate their respective fair values due to their short-term nature. The Company uses a three-tier fair value hierarchy to classify and disclose all assets and liabilities measured at fair value on a recurring basis and to minimize the use of unobservable inputs when determining their fair value. The three tiers are defined as follows:

Level 1—Observable inputs based on unadjusted quoted prices in active markets for identical assets or liabilities

Level 2—Inputs, other than quoted prices in active markets, that are observable either directly or indirectly

Level 3—Unobservable inputs for which there is little or no market date, which require the Company to develop its own assumptions

The Company classifies investments in money market funds within Level 1 as the prices are available from quoted prices in active markets. Investments in repurchase agreements are classified within Level 2 as these instruments are valued using observable market inputs including reported trades, broker/dealer quotes, bids and/or offers.

As of December 31, 2019 and December 31, 2018, the Company held cash equivalents which are composed of money market funds and repurchase agreements that were purchased through repurchase intermediary banks and collateralized by deposits in the form of government securities and obligations.

The following represents assets measured at fair value on a recurring basis by the Company (in thousands):

December 31, 2019	Fair Value	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 3,395	$ 3,395	$ —	$ —
Repurchase agreements	173,000	—	173,000	—
	$ 176,395	$ 3,395	$ 173,000	$ —

December 31, 2018	Fair Value	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 781	$ 781	$ —	$ —
Repurchase agreements	94,500	—	94,500	—
	$ 95,281	$ 781	$ 94,500	$ —

NOTE 12: COLLABORATION AND LICENSE AGREEMENTS

Development and Commercial License Agreement with Servier

On February 24, 2016, the Company entered into a development and commercial license agreement, as subsequently amended, with predecessor entities to Servier. This agreement establishes a collaboration between the Company and Servier to develop allogeneic chimeric antigen receptor T ("CAR T") cell therapies for up to six unique antigen targets selected by Servier. Servier selected one target at the agreement's inception. Servier is required to make a milestone payment to the Company upon achievement of an early-stage pre- investigational new drug application ("IND") development milestone event completed for each of the remaining five targets selected, if any. The Company granted Servier a development license and will perform early-stage R&D on the selected targets and develop the resulting therapeutic product candidates through Phase 1 clinical trials and manufacture clinical trial material for use in Phase 2 clinical trials. Also, the Company and Servier have formed a joint steering committee ("JSC") to provide high-level oversight and decision making regarding the activities covered under the agreement.

The Company received an upfront payment of $105.0 million under the agreement. At the Phase 2 readiness stage for any product candidate, Servier may exercise a commercial option, subject to payment of commercial option exercise fees, to proceed with development and commercialization of the product candidate and perform late-stage R&D, including Phase 2 and Phase 3 clinical trials and obtaining regulatory approvals. The Company has the ability to receive total payments, in the aggregate across all six targets that may be selected by Servier, of up to approximately $1.6 billion, including the upfront payment of $105.0 million and up to $1.5 billion in milestone payments, consisting of up to $401.3 million in development milestone payments and up to $1.1 billion in commercial milestone payments. The Company is also entitled to receive tiered royalties ranging from the mid-single digit percentages to the sub-teen percentages on worldwide net sales of any products developed, subject to customary potential reductions. The Company also has the right to opt in and participate in the development and commercialization of any products resulting from the collaboration through a 50/50 codevelopment and co-promotion option in the United States. This will require the Company to pay a codevelopment and co-promotion option fee on each licensed product for which the Company elects to participate. This option is exercisable at the Phase 2 readiness stage and only after Servier exercises its commercial option.

The Company assessed this arrangement in accordance with ASC 606 and concluded that the promises in the agreement represent transactions with a customer. The Company has determined that the promises associated with the research and development activities for each of the six targets are not distinct because they are all based on the ARCUS proprietary genome editing platform. The Company has concluded that the agreement with Servier contains the following promises: (i) a development license; (ii) performance of early-stage R&D services, (iii) the manufacture of clinical trial material for use in Phase 2 clinical trials, and (iv) JSC participation. The Company determined that the license, manufacture of clinical trial material, and R&D services were not distinct from each other, as the license, pre-clinical and clinical supply, and R&D services are highly interdependent upon one another. Participation on the JSC to oversee the research and development activities are combined into the single performance obligation as these activities are highly interdependent with the other R&D services. As such, the Company determined that these promises should be combined into a single performance obligation.

Under the agreement with Servier, in order to evaluate the appropriate transaction price, the Company determined that the upfront amount of $105.0 million constituted the entire consideration to be included in the transaction price as of the outset of the arrangement. As such, this amount was allocated to the single performance obligation. The commercial option exercise fees that may be received are excluded from the transaction price until each customer option is exercised as it was determined that the options are not material rights. The potential development milestone payments that the Company is eligible to receive prior to the exercise of the options as well as commercial milestones, were excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement, since the milestones relate to successful achievement of certain developmental goals, which might not be achieved. None of the future royalty payments were included in the transaction price, as the potential payments represent sales-based consideration. The Company will reevaluate the transaction price, including all constrained amounts, at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

The Company recognizes revenue from the upfront payment of $105.0 million based on an input method in the form of research effort relative to expected research effort at the completion of the performance obligation, which is based on the actual time of R&D activities performed relative to expected time to be incurred in the future to satisfy the performance obligation. Management evaluates and adjusts the total expected research effort for the performance obligation on a quarterly basis based upon actual research accomplishments and the probability of continuing research efforts in the future. The transfer of control occurs over this time period and, in management's judgment, is the best measure of progress towards satisfying the performance obligation. The remaining performance obligation associated with the $105.0 million upfront payment is expected to be satisfied over a four year period as of December 31, 2019.

During the years ended December 31, 2019 and December 31, 2018, the Company recognized revenue under the agreement with Servier of approximately $7.3 million and $5.8 million, respectively. Deferred revenue related to the agreement with Servier amounted to $80.9 million and $88.6 million as of December 31, 2019 and December 31, 2018, respectively, of which $15.0 million and $5.8 million, respectively is included in current liabilities. No development or sales-based milestone payments were received during the year ended December 31, 2019 and December 31, 2018.

Collaboration and License Agreement with Gilead

On September 10, 2018, the Company and Gilead Sciences, Inc. ("Gilead") entered into a collaboration and license agreement to develop genome editing tools to target viral DNA associated with Hepatitis B. Pursuant to the terms of the agreement, Gilead will receive an exclusive license to exploit the resulting synthetic nucleases and products that use them to treat Hepatitis B in humans ("development license"), and the Company is entitled to receive up to $40.0 million in research funding for early-stage R&D services, paid in semi-annual increments, over an initial three year term and development and commercial milestone payments of up to an aggregate of $445.0 million, consisting of up to $105.0 million in development milestone payments and up to $340.0 million in

commercial milestone payments. The Company is also entitled to receive tiered royalties ranging from the high single digit percentages to the mid-teen percentages on worldwide net sales of the products developed through the term of the agreement, subject to customary potential reductions. Gilead is responsible for obtaining regulatory approvals and, upon completion of the collaboration, will assume sole responsibility for the development and commercialization of such gene editing therapies and products. The Company will provide technology transfer of its development know-how prior to Gilead assuming responsibility. Also, the Company and Gilead will negotiate a separate supply agreement for the Company to manufacture specifically identified products for Gilead to use in clinical trials at price based on the Company's costs. The Company and Gilead have formed a joint steering committee ("JSC") and a joint research and development committee ("JRDC") that collectively will provide oversight, decision making and implementation guidance regarding the collaboration activities covered under the agreement.

The Company assessed this arrangement in accordance with ASC 606 and concluded that the promises in the agreement represent transactions with a customer. The Company has concluded that the agreement with Gilead contains the following promises: (i) a development license; (ii) performance of early-stage R&D services, including technology transfer services, iii) JSC and JRDC participation, and (iv) regulatory responsibilities related to non-clinical and chemistry, manufacturing and control ("CMC") reports. The Company determined that the license and R&D services were not distinct from each other, as the license and R&D services are highly interdependent upon one another. Participation on the JSC and JRDC to oversee the research and development activities are combined into the single performance obligation as these activities are highly interdependent with the other R&D services. The regulatory responsibilities related to non-clinical and CMC filings do not represent separate performance obligations based on their dependence on the research and development efforts. As such, the Company determined that these promises should be combined into a single performance obligation.

Under the agreement with Gilead, in order to evaluate the appropriate transaction price, the Company determined that the $40.0 million research funding for early-stage R&D services, paid in semi-annual increments over an initial three-year term, constituted the entire consideration to be included in the transaction price as of the outset of the arrangement. As such, this amount was allocated to the single performance obligation. The potential development and commercial milestone payments that the Company is eligible to receive were excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement, since the milestones relate to successful achievement of certain developmental goals, which might not be achieved. None of the future royalty payments were included in the transaction price, as the potential payments represent sales-based consideration. The Company will reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

Revenue associated with the combined performance obligation is being recognized as revenue on a straight-line basis as the R&D services are provided over the initial three-year term. The transfer of control occurs over this time period and, in management's judgment, is the best measure of progress towards satisfying the performance obligation.

During the years ended December 31, 2019 and December 31, 2018, the Company recognized revenue under the agreement with Gilead of approximately $13.3 million and $3.7 million, respectively. Deferred revenue related to the agreement with Gilead amounted to $1.5 million and $2.3 million as of December 31, 2019 and December 31, 2018, respectively, all of which is included in current liabilities. No development or sales-based milestone payments were received during the year ended December 31, 2019.

Research, Collaboration and License Agreement with the Trustees of the University of Pennsylvania

On January 1, 2018, the Company entered into a Research, Collaboration and License Agreement with the University of Pennsylvania ("Penn") to collaborate on the preclinical development for gene editing products involving the delivery of an ARCUS nuclease. The Company will provide semi-annual research funding payments of up to $5.0 million for a three-year term to fund the cost of research programs as specified in a mutually agreed-upon research budget and be responsible for post-IND enabling study development activities. The research funding payments will be expensed as incurred; however, if payments made by the Company exceed the costs incurred by Penn in the six-month period, the excess amount will be credited to the Company in the next semi-annual period.

In addition to the research funding payments, if the Company elects to use certain Penn technology, the Company will be required to make development and sales milestone payments totaling up to $16.1 million per product in any one year, assuming the maximum development and sales milestones are met in any one year. An additional $12.3 million per product in sales milestone payments could be payable in other years if other sales thresholds are achieved, thus totaling $28.4 million in aggregate milestone payments per product. Low single-digit royalty percentages are also payable on net sales of certain products.

Penn provided the Company a non-exclusive license for patent rights and know-how to be used in exchange for an upfront payment of $0.3 million. Once the Company has paid $15.0 million in research funding, it then has the option to pay a $1.0 million option fee to obtain a license for additional patent rights.

In October 2019, both parties agreed to adjust the activities conducted under the agreement to focus exclusively on the collaboration's program to edit the PCSK9 gene to reduce levels of LDL-C in the blood, commonly known as "bad cholesterol". The agreement's termination provisions allow the Company to terminate the agreement by providing written notice at least 60 days prior to the due date of the next semi-annual research funding payment. In this event, the Company would not make termination payments to Penn other than for non-cancelable costs and reasonable wind-down costs.

NOTE 13: SEGMENT REPORTING

The Company has developed a genome editing platform and performed related research for human therapeutic and agricultural applications. The Company's Chief Operating Decision Maker ("CODM") evaluates the Company's financial performance based on two reportable segments: Therapeutics and Food. The Therapeutics segment is focused on the development of products in the field of immuno-oncology and of novel products outside immuno-oncology to treat human diseases. The Food segment is focused on applying ARCUS to develop food and nutrition products through collaboration agreements with consumer-facing companies. The CODM reviews segment performance and allocates resources based upon segment revenue and segment operating loss of the Therapeutics and Food reportable segments.

Segment operating loss is derived by deducting operational cash expenditures, net, from GAAP revenue. Operational cash expenditures are cash disbursements made that are directly attributable to the reportable segment (including directly attributable research and development and property, equipment, and software expenditures). For the year ended December 31, 2018, the Company allocated centralized research and development expenditures for early stage research, nuclease development and the purchase of general laboratory supplies to the Therapeutics and Food segments based on headcount. In January 2019, the Food segment moved into a new leased facility in Durham, North Carolina. The Company has determined that the Food segment is no longer deriving benefit from the Company's centralized research and development expenditures, thus all these expenditures are allocated to the Therapeutics segment for the year ended December 31, 2019. The reportable segment and centralized research and development operational cash expenditures include cash disbursements for compensation, laboratory supplies, purchases of property, equipment, and software and procuring services from CROs, CMOs, and research organizations.

Certain cost items are not allocated to the Company's reportable segments. These cost items primarily consist of compensation and general operational expenses associated with the Company's executive, business development, finance, operations, human resources and legal functions. The Company does not allocate non-cash income statement amounts to its reportable segments, such as share based compensation, depreciation and amortization, intangible asset impairment charges, non-cash interest expense and losses on the disposal of assets. When reconciling segment operating loss to consolidated loss from operations, the Company makes an adjustment to convert the cash expenditures to the accrual basis to reflect GAAP.

All segment revenue is earned in the United States and there are no intersegment revenues. Additionally, the Company reports assets on a consolidated basis and does not allocate assets to its reportable segments for purposes of assessing segment performance or allocating resources.

Presented below is the financial information with respect to the Company's reportable segments

(in thousands)	Years Ended December 31, 2019	2018
Revenue:		
Therapeutics	$ 20,632	$ 9,523
Food	1,606	1,360
Total segment revenue	22,238	10,883
Segment operational cash expenditures:		
Therapeutics	$ 45,941	$ 35,045
Food	6,984	9,125
Total segment operational cash expenditures	52,925	44,170
Allocation of centralized research and development operational cash expenditures:		
Therapeutics	$ 24,118	$ 11,605
Food	—	2,901
Total allocation of centralized research and development operational cash expenditures	24,118	14,506
Segment operating loss:		
Therapeutics	$ (49,427)	$ (37,127)
Food	(5,378)	(10,666)
Total segment operating loss	(54,805)	(47,793)
Adjustments to reconcile segment operating loss to consolidated loss from operations:		
Corporate general and administrative cash expenditures	$ (32,569)	$ (15,892)
Interest income received	(4,267)	(1,875)
Depreciation and amortization	(5,317)	(2,354)
Share-based compensation	(8,940)	(2,453)
Loss on disposal of assets	(22)	(14)
Adjustments to reconcile cash expenditures to GAAP expenses	18,716	22,469
Total consolidated loss from operations	$ (87,204)	$ (47,912)

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Executive Officers

Matthew Kane
President, Chief Executive Officer and Director

Derek Jantz, Ph.D.
Chief Scientific Officer and Director

Abid Ansari
Chief Financial Officer

Christopher Heery, M.D.
Chief Medical Officer

Dario Scimeca
General Counsel and Secretary

Fayaz Khazi, Ph.D.
Chief Executive Officer, Elo Life Systems

David Thomson, Ph.D.
Chief Operating Officer

Board of Directors

Kevin Buehler
Chairman of the Board of Directors, Former Division Head, Alcon Laboratories Inc.

Geno Germano
President and Chief Executive Officer, Elucida Oncology, Inc.

Derek Jantz, Ph.D.
Chief Scientific Officer, Precision BioSciences, Inc.

Matthew Kane
President and Chief Executive Officer, Precision BioSciences, Inc.

Raymond Schinazi, Ph.D., DSc
Frances Winship Walters Professor of Pediatrics and Director of Laboratory of Biochemical Pharmacology, Emory University

Shalini Sharp
Executive Vice President and Chief Financial Officer, Ultragenyx Pharmaceutical Inc.

Tony Yao, M.D., Ph.D.
Portfolio Manager, ArrowMark Partners

Corporate and Stockholder Information

Corporate Headquarters
Precision BioSciences, Inc.
302 East Pettigrew Street, Suite A-100
Durham, North Carolina 27701
www.precisionbiosciences.com

Transfer Agent
American Stock Transfer & Trust Company
6201 15th Avenue
Brooklyn, NY 11219
Phone: 800.937.5449
www.amstock.com

Investor Relations
Nick Riddle, M.D., Ph.D.
Vice President, Financial Strategy and Investor Relations
IR@precisionbiosciences.com

Annual Meeting of Stockholders
Wednesday, May 13, 2020
11:00 a.m., Eastern Time
Via live webcast

Common Stock Listing
Nasdaq: DTIL

Corporate Counsel
Latham & Watkins LLP
885 Third Avenue
New York, NY 10022-4834
Phone: 212.906.1200
www.lw.com

Independent Registered Public Accounting Firm
Deloitte & Touche LLP

PRECISION
BIOSCIENCES

302 East Pettigrew St.
Suite A-100
Durham, NC 27701

www.precisionbiosciences.com